



UNIVERSITY OF THESSALY
SCHOOL OF SCIENCE
DEPARTMENT OF COMPUTER SCIENCE AND
BIOMEDICAL INFORMATICS

**Systematic review, field synopsis and meta-analysis to determine
bioactivity of chemical compounds of hop (*Humulus lupulus*).**

Despoina Kiofentzoglou

DIPLOMATIC THESIS

Supervisor

Greta Braliou



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Με ατομική μου ευθύνη και γνωρίζοντας τις κυρώσεις ⁽¹⁾, που προβλέπονται από της διατάξεις της παρ. 6 του άρθρου 22 του Ν. 1599/1986, δηλώνω ότι:

*Δεν παραθέτω κομμάτια βιβλίων ή άρθρων ή εργασιών άλλων αυτολεξεί **χωρίς να τα περικλείω σε εισαγωγικά** και χωρίς να αναφέρω το συγγραφέα, τη χρονολογία, τη σελίδα. Η αυτολεξεί παράθεση χωρίς εισαγωγικά χωρίς αναφορά στην πηγή, είναι λογοκλοπή. Πέραν της αυτολεξεί παράθεσης, λογοκλοπή θεωρείται και η παράφραση εδαφίων από έργα άλλων, συμπεριλαμβανομένων και έργων συμφοιτητών μου, καθώς και η παράθεση στοιχείων που άλλοι συνέλεξαν ή επεξεργάστηκαν, χωρίς αναφορά στην πηγή. Αναφέρω πάντοτε με πληρότητα την πηγή κάτω από τον πίνακα ή σχέδιο, όπως στα παραθέματα.*

*Δέχομαι ότι η αυτολεξεί **παράθεση χωρίς εισαγωγικά**, ακόμα κι αν συνοδεύεται από αναφορά στην πηγή σε κάποιο άλλο σημείο του κειμένου ή στο τέλος του, είναι αντιγραφή. Η αναφορά στην πηγή στο τέλος π.χ. μιας παραγράφου ή μιας σελίδας, δεν δικαιολογεί συρραφή εδαφίων έργου άλλου συγγραφέα, έστω και παραφρασμένων, και παρουσίασή τους ως δική μου εργασία.*

Δέχομαι ότι υπάρχει επίσης περιορισμός στο μέγεθος και στη συχνότητα των παραθεμάτων που μπορώ να εντάξω στην εργασία μου εντός εισαγωγικών. Κάθε μεγάλο παράθεμα (π.χ. σε πίνακα ή πλαίσιο, κλπ), προϋποθέτει ειδικές ρυθμίσεις, και όταν δημοσιεύεται προϋποθέτει την άδεια του συγγραφέα ή του εκδότη. Το ίδιο και οι πίνακες και τα σχέδια

4. Δέχομαι όλες τις συνέπειες σε περίπτωση λογοκλοπής ή αντιγραφής.

Ημερομηνία:/.../20...

Ο – Η Δηλ.

(Υπογραφή)

(1) «Όποιος εν γνώσει του δηλώνει ψευδή γεγονότα ή αρνείται ή αποκρύπτει τα αληθινά με έγγραφη υπεύθυνη δήλωση του άρθρου 8 παρ. 4 Ν. 1599/1986 τιμωρείται με φυλάκιση τουλάχιστον τριών μηνών. Εάν ο υπαίτιος αυτών των πράξεων σκόπευε να προσπορίσει στον εαυτόν του ή σε άλλον περιουσιακό όφελος βλάπτοντας τρίτον ή σκόπευε να βλάψει άλλον, τιμωρείται με κάθειρξη μέχρι 10 ετών.

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**Συστηματική ανασκόπηση, σύνοψη πεδίου και μετα-ανάλυση για
τον προσδιορισμό βιοδραστηκότητας των χημικών ενώσεων του
λυκίσκου (*Humulus lupulus*).**

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Science and Biomedical Informatics,
University of Thessaly

Παναγιώτα Κοντού

Παντελής Μπάγκος

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Abstract

INTRODUCTION: *Humulus lupulus*, commonly named hops, is a climbing plant which is used mainly in brewing factory in order to maintain and enhance the flavor of the beer. Its female cones are responsible for bitter taste, aromatic flavor and a variety of benefits in humans, like sedative, estrogenic, anticancer, antiinflammatory and antioxidant. In the present study, we analyze the antimicrobial activity of hop compounds and extracts against different microorganism, through meta-analysis, by calculating the MIC (Minimum Inhibitory Concentration) value.

MATERIALS AND METHODS: An extended literature search was performed to find all studies referring to antimicrobial activity of hop. For each article, which was eligible for our study, we recorder information about strains, hop compounds, hop extracts, time of incubation (24, 48 hours), temperature, number of replicates and MIC along with its standard deviation. The data were divided into three classes of hop compounds and extracts. Meta-analysis was performed using StataSE13.1.

RESULTS: A total of 2553 articles were retrieved from the literature search, of which the 18 met all the criteria for the meta-analysis process. The total number of reports from those articles were 450 and among those studies we found 6 compounds and 3 extracts, as well as 55 strains. Finally, 174 of those reports have 24 hours incubation, while 276 have 48 hours.

CONCLUSIONS: In 48h incubation, flavonoids have better antimicrobial activity than bitter acids against different microorganisms. Flavonoids and bitter acids seem to have similar antimicrobial activity in probiotic, pathogenic and food spoilage microorganisms.

1. Chapter 1: Introduction

1.1 Humulus Lupulus

Humulus lupulus, the common hops, is a dioecious climbing plant belonging to the genus *Humulus* in the family of the Cannabinaceae [1]. *Humulus lupulus* is used mainly in brewing factory in order to maintain and enhance the flavor of the beer. It is believed that *Humulus* started from China.

It climbs in a clockwise direction around any available support, can reach the height of up to 10m living up to 20 years and has a diameter of about 1 cm with hexagonal section. Roots are large, reaching up to 100m in one growing season and requires a deep, well-drained fertile soil while its leaves are usually with color green to yellowish-brown, have 3 to 5 lobes with serrate margins [2]. Hops has female and male flowers growing usually in separate plants. The cones of female plants are called strobili with 2.5-5 cm length and have overlapping bracts been found on the central axis. Moreover, the seeds, which contains 33% fats and oils, are small, hard, and waterproof but with no brewing value as they negatively affect the taste of the beer [2]. When the stipules and the bracts, which contains polyphenols, are separated, these constitute the drug lupulin, which the odor and taste is due mainly to the very complex secretion contained in the lupulin glands. The last ones are only weakly attached to the hop flower and that means that the hops have to be handled carefully in order not to lose the lupulin. On the other hand, the male plants are very rare in the wild, they don't produce cones and in case of existence of a male plant, it should be eliminated immediately because it will pollinate all the female plants [3].

It grows mainly from the end of April to the beginning of July in the temperate climate zone. Approximately by June the plant is 3-4m tall and in August the height increases to 6-10m, therefore ready to be harvest [4]. A second important feature of the blossom is the length of the day and supplementarily the latitudes which is 38° to 51°. Too far south the days are too short and too far north the climate is adverse and that's why in North America is primarily cultivated in areas like Washington and in Europe in Germany, Great Britain, Poland and Czech Republic [1]. A daily analysis for α -acids from the cones can determine the best period for picking the flowers as well as the weather conditions and the visual examination of the cones [4].



Figure 1: female hop's cone



Figure 2: Plant of *Humulus Lupulus* (hop)

There are numerous different species of *Humulus lupulus*, but currently four of them are recognized. They are distinguished from the density of hair on the leaf and density of glands on the lower leaf surface.

- *Humulus lupulus* is the hops for beer making been cultivated in Europe.
- *Humulus lupulus* var. *neomexicanus* is cultivated in North America.
- *Humulus lupulus* var. *pubescens* is cultivated in North America, Minnesota.
- *Humulus lupulus* var. *lupuloides* is cultivated in North America, Minnesota as well [5].

Lately the use of hops except for the brewing is under research in order to find out promising medical usages of the plant or confirmations to already existing studies.

1.1.1 History

Hops full name as it is referred before, is *Humulus Lupulus* (Greek word: λυκίσκος). The origine of the word “Humulus” has not been found yet, but it is assumed that it is proto-Iranian, while by the word *Lupulus*, which means small wolf in the Latin vocabulary, it is shown the climbing behavior of the plant as well as the suffocation of other plants by hops. It is acceptable that the first connection between beer and hops is refereed in 822 in a manuscript of Abbot Adalhard Benedictine monastery of Corbie in Germany and then in 1067 by abbess Hildegard of Bingen. There is also evidence that beer was produced during the Pre-Pottery Neolithic era around 8500 BC. The beginning of cultivation of

hops is still unclear, but it is considered that it appears to Bavaria where there is still the largest single hop-cultivating area. After that, England has grown hops approximately at the years 1511 to 1524 in Kent, despite the fact that after two hundred years it said that in Massachusetts it was grown the first commercial hop. [6]

1.1.2 Chemical composition

There are mainly two types of metabolites in almost every plant but also in the hop too, the primary and the secondary. The first ones are related to the growth and maintenance of the organism to help each plant with the normal survival activities. So, the basic primary metabolites are the vitamins, nucleotides, ethanol, lactic acid and specific types of amino acids. Secondary metabolites, which play the most important role in the hop, are formed when primary metabolites are modified, and their role is to be a part in ecological activities such as defense mechanisms and antibiotics. Hop's most important secondary metabolites are bitter acids, oils and polyphenols mostly flavonoids and play a significant role to beer's flavor, aroma and bitterness [7]. In hop the secondary metabolites are produced in the lupulin glands of the female hop flowers. Finally, the aroma depends on the technology been used during the brewing process [8].

1.1.2.1 *Bitter acids*

Bitter acids, been named like that because they are responsible for the bitter flavour in the beer, contain prenylated acylphloroglucinols and prenylchalcones. The first ones include the α -acid which refers to humulone and its acyl-side chain the cohumulone and adhumulone which are the major analogues as well as the posthumulone, prehumulone and adprehumulone which are minor analogues [9]. Approximately 50-60% of α -acids go through thermal isomerization during wort boiling that leads to iso- α -acids. Lack of isomerization can be caused due to the limited solubility of the α -acids [10]. β -acids such as lupulone, colupulone and adlupulone are also part of the bitter acids content and their differences from the α -acids is that they have an extra dimethylallyl prenyl group but also they cannot isomerize the same way as the α -acids. The most important process happening in β -acids is oxidation by airborne oxygen which is happening during natural ageing [10]. To be more precise α -acids give beer her bitterness mostly when they are isomerized and as a result the longer the boiling time is, the bitterness will be increased. Beta acids are not important in the brewing process due to the fact that they have a low solubility in water, but they are important when you have to calculate the ratio between them and α -acids. Usually the aroma varieties have 1:1 Alpha to Beta acids ratio and the most bittering hops have 3:1 ratio or even more [11].

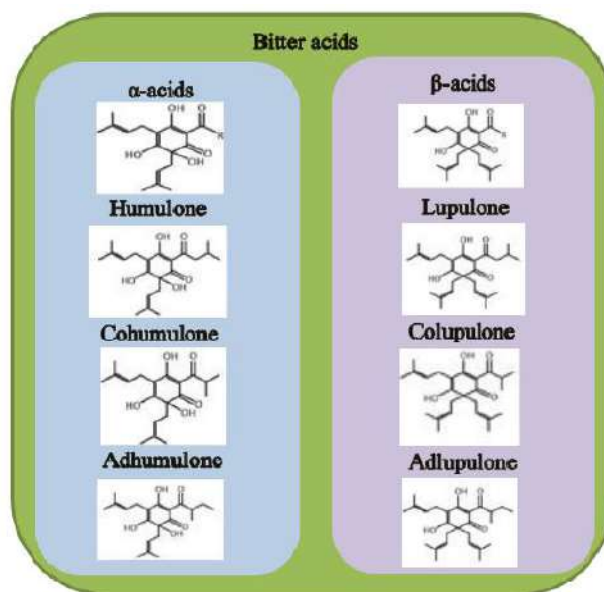


Figure 3: Division of bitter acids. α -acids in the left side, β -acids in the right side and images of chemical composition

1.1.2.2 Polyphenols

Hop polyphenols are a group of secondary metabolites, as we referred before, with a huge variety, which is observable from the fact that there are about 100 polyphenolic substances in hop cones. There are generally in the green part of cone and in the amount of three to eight percent. Flavonoids belongs to non-glycosylated form of polyphenols and consists of flavan-3-ols ((+)-catechin, (-)-epicatechin), flavones, flavonols and prenylflavonoids (isoxanthohumol, xanthohumol). The last one basically, belongs to the group of prenylated chalcones [9]. Flavonoids are also known for their functions, antioxidants, antimicrobials, having a flavan molecule derived from the heterocyclic structure by substitution of its C ring in position 2 or 3 with a phenyl group. If the C ring is in position 2 it is classified as flavones and if it is in position 3 it is classified as isoflavones.

Chalcones are one of the most important secondary metabolites, in which two aromatic rings are linked by an aliphatic three-carbon α,β -unsaturated system. Two examples of chalcones are xanthohumol and isoxanthohumol, which are both formed in female flowers. Xanthohumol is formed in lupulin glands by a biosynthesis which includes prenylation and O-methylation of the polyketide intermediate chalconaringenin. Mostly in beers the content of xanthohumol is around 0.1-1% (dry weight), but it depends on the cultivar and the climate in which the hop grows. In commercial beers there are about 0.002-0.690 mg/L xanthohumol, while the concentration of isoxanthohumol appears to be around 0.040-0.716 mg/L. The method that was used to determine xanthohumol in hops was high-performance liquid chromatography using UV detection. However, the usage of tandem mass spectrometry simultaneously with liquid chromatography has more sensitivity to prenylflavonoids than the previous method. [12]

Isoxanthohumol belongs to prenylated flavanones and consists of two hydroxyl groups at C-7 and C-4' and the prenyl group at C-8. It can be metabolized to human liver to form 8-prenylnaringenin, as a result of the O-demethylation reaction. [12] Isoxanthohumol appears to be more than xanthohumol during brewing process because of the wort boiling process, which means thermal isomerization of chalcones into flavanones. It is important to refer that, isoxanthohumol was also found in non-alcoholic beer at a concentration of 0.11 mg/L.

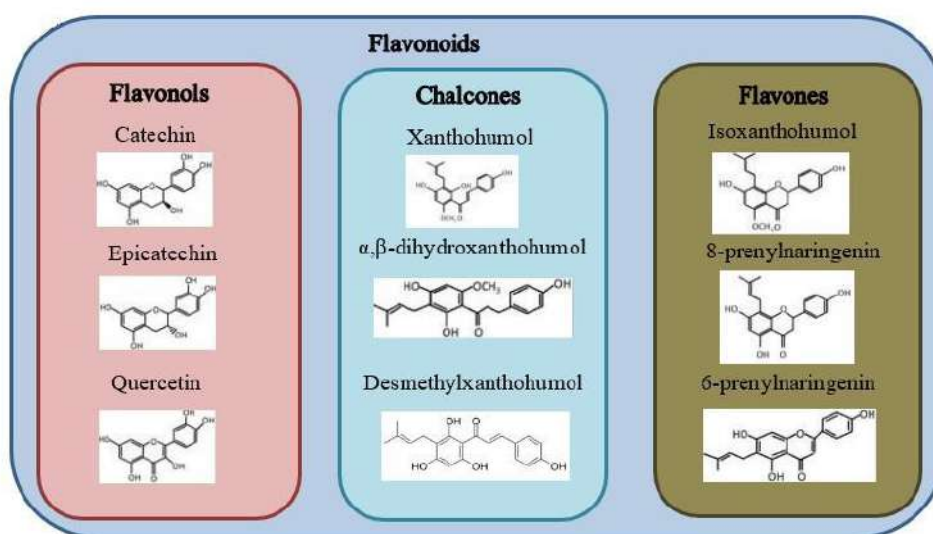


Figure 4: Division of flavonoids. Flavonols in the left side, chalcones in the centre and flavones in the right side with their chemical composition

1.1.2.3 Essential oils

Essential oils are also a significant part of hops, belonging to the secondary metabolites and their role is the characteristic aroma and taste of hop and consequently of beer. Oils are found in flowers with a concentration from about 0.4 to 2.5 mL/100g steam volatile and they are exported from a two hour process called hydrodistillation [13]. To be more clear, essential oils tend to enhance hop flavor without any extra bitterness, increases the beer yeast using less vegetative materials [14] but also, they have the same solubility both in hot and cold side, which is very convenient for the researchers [15]. Hop oils can be added either pre- or post-filtration, fact that plays a significant role in their flavor and aroma.

The essential oils contain terpenes, sesquiterpenes and their respective oxygenated derivatives, esters, ketones as well as thiols [16]. Terpenes have about 0.5-3% of the total hop weight and the most common are the monoterpene myrcene and sesquiterpenes caryophyllene, been known for their high insolubility in water. Myrcene referred as the most odor active component, giving the herbaceous aroma and can reach

up to 70% w/v of the essential oils. Sesquiterpenes are a subclass of terpenes been playing a significant role on the central nervous system. Sesquiterpenes caryophyllene tastes spicy but also sweet, which means that it contributes to the beer's flavour, depending on the hop variety but also the weather conditions [17].

The most common way to extract oils from hops is distillation. There are different solvents, which are used to dissolve hops, such as ethanol, carbon dioxide (CO₂ extract), water and supercritical fluids (SCF). The first one is known as a polar solvent and is suitable for polyphenols, leading to a very high significance result, because the extract seems like the hops itself. The second one, CO₂ extract is the most used one among breweries because when it is used, there is lack of traces of undesired organic solvents, but water as well is used as medium solvent especially for organic compounds [12]. Last but not least, supercritical fluid extraction is used to volatile and nonvolatile compounds. Even though high percentage of volatile compounds appear at lower temperatures and bitter acids appear at higher temperatures, under the conditions which are used most of the prenylflavonoids remain in the hops.

1.1.3 Hop contribution to beer

There are mostly four usages of hops to beer, which are bitterness, aroma, microbial stability and foam.

1.1.3.1 Bitterness

Bitterness is a characteristic of beer, which is one of the most distinguishable aftertaste that has the consumer after drinking it. This is a result of a thermal isomerization of α -acids into iso- α -acids, being happening during wort boiling. Additionally, cis is and trans forms are products of the yield of α -acids into two iso- α -acids, from which the first one is more bitter than the latest. Iso- α -acids offer approximately the 85% of the bitterness, while the other 15% is a result of hop polyphenols and oxidation of β -acids. [18]

1.1.3.2 Aroma

Aroma is a very complex component of the beer, because not until the usage of gas chromatography, were not investigators capable of finding the contribution of hop oils. After 90 minutes of boiling, almost 95% of the oils has evaporated, because they are high volatile and poorly soluble and the other 5% has transformed into their polymerized form. Those who remain unchanged during the whole process were found after many studies to be β -myrcene, methyl, ketone and α -humulene. No one of them can offer the aroma itself, but it is a result of combination, in order to give the fruity, floral, citrus, grassy and spicy notes, which make every beer distinguish from the others. [18]

1.1.3.3 Microbial stability

In order to fully understand the mechanism behind the microbial stability of hops we need to research hop bitter acids. They play a significant role in the preservative properties of beer, because they protect beer from infections. Later it was found that Gram-positive bacteria restrict the antibiotic properties of hops, while the negative ones were unaffected by the bitter acids. Shimwell, [19] observed that bitter acids develop an antiseptic capacity at lower pH values, while even the smallest fluctuation in pH can cause changes in the antibacterial role of bitter acids. Those changes can be caused by ionophores, having many consequences like lack of nutrient transport and starvation of the organism.

Through some studies, it is found that beer spoilage lactic acid bacteria have a significant character, which is the resistance to bitter acids, having as well many defense mechanisms. Sami et al. [20] have found that *horA* is a gene being responsible for the resistance. After collecting the data and having some research, it was found that cell walls and cytoplasmic membranes have a significant role in the defense being referred earlier.

1.1.3.4 Foam

Another important feature of beer, according to MEBAK (Mittleeuropäischen Brautechnischen Analysenkommission) [21] is the foam stability, which is formed from iso- α -acids, derived from α -acids, as researches have shown. Hydrophobicity is the key behind the stabilization of beer because those compounds concentrate in the foam.

1.1.4 Benefits of hops in humans

1.1.4.1 Sedative activity

Despite the fact that surveys, that confirm the presence of sedative activity, are few recently some of them indicate that hops and especially non-alcoholic beers help anxiety and sleep disorders in humans. Women who worked in hospital were the object of studies and the results show that hops did not affect their duration of sleep but the quality and the decrease of anxiety during it. It is believed that these effects are connected with an increase in GABA_A receptor function, because humulone may act as positive modulator of GABA_A receptors at low micromolar concentrations. [22]

1.1.4.2 Support effects on menopausal symptoms

A typical process in the woman body is menopause, which tends to appear in older women. The main symptoms are hot flushes, night sweats, sleep disturbances and fatigue due to estrogen deficiency. Despite the fact that the most common therapy for most of the symptoms is HRT, which is combination of estrogens with progestins, hormonal substitution, in 2002 Woman's Health Initiative (WHI) have found that it can cause breast cancer and thromboembolism as well. Many recent in-vivo researches have found that 8-prenylnaringenin (8-PN) in hops is one of the most potent phytoestrogens and can help women with menopausal and post-menopausal symptoms. It seems that 8-PN has two-fold higher affinity for ER α than ER β after many in vitro assays, while it is observed that phytoestrogens structure tend to be almost the same with 17 β -estradiol, which is generated by ovaries and that is one reason why it is helping. [23]

1.1.4.3 Antimicrobial activity

It is shown that the antimicrobial activity of hops derives from the activity of it, which can decrease the function of many mechanisms in bacteria, fungi and parasites. Antibacterial activity is enhanced by bitter acids, and in particular α -acids and β -acids and is applied mainly to Gram-positive bacteria strains such as Staphylococcus, Streptococcus, Micrococcus and Mycobacterium. Despite the fact that Gram-negative bacteria have not resistance, lupulone was found to show antibacterial activity against plenty of them. Bitter acids also contribute to antifungal activity of hops but also xanthohumol and 6-prenylnaringenin reacts against Trichophyton mentagrophytes and T. rubrum. Finally, some researches also found that it has potential antiviral and antiparasitic effects and especially xanthohumol against bovine viral diarrhea virus (BVDV) for the former and chalcones against Plasmodium for the latter. [24]

1.1.4.4 Anticancer activity

As studies show, xanthohumol interacts with many cancers, from lung and digestive to endocrine or genito-urinary system, leukemia, and skin. This effect is possible due to inhibitory action on two signaling pathways, Akt, NF-kB, being responsible for expression of genes involved in cancer cell survival, proliferation, invasion, angiogenesis, metastasis and radioresistance. Thus we can observe that xanthohumol is a multitargeted agent, having autophagic, proapoptotic and chemopreventive effects to cancer cells. [25]

1.1.4.5 Other activities

There are some important activities too like antiobesity, skin and hepatic protection. Studies show that xanthohumol has results referring to effects of both antiobesity and antiglycemic, because the conclusion of these studies indicate a grow in lipolysis and break down of fatty acids by enhancing beta oxidation in adipocytes when there was treatment with xanthohumol. Beta oxidation is possible to be proliferated through

activation of the AMPK signaling pathway. [26] Furthermore, applications of xanthohumol in dermatology can lead to treatment of atopic eczema, dermatitis, pigment disorders, skin infections, skin ageing, skin cancers and photo protection. The results of in vivo researches referring to liver illustrate that diseases like non-alcoholic steatohepatitis and expression of profibrogenic genes, when they are fed with xanthohumol, decline hepatic inflammation. [27]

1.2 Antimicrobial

1.2.1 Minimum inhibitory concentration (MIC)

The lowest concentration of a chemical which is usually a drug and has as a result the end of bacterial or fungi growth after overnight incubations, is called Minimum Inhibitory Concentration (MIC). It is mainly used in diagnostic labs in order to detect the grade of resistance which is based on already known values called breakpoints. MIC can also contribute to more successful treatments because it can help in the usage of the right drug and amount of it. Simultaneously with the MIC value we should know the pharmacokinetic parameters (PK) which are referred to the drug in the host organism. [28] Those parameters involve volume of distribution (Vd), elimination half-life ($t_{1/2}$) and clearance.

There are two methods to determine the MIC values, the dilution, and the gradient. The first one is divided into agar and broth dilution. Agar method uses nutrient agar surfaces, which are full of varying antibiotic concentrations, in order to drop solutions with bacterial cells and look after overnight incubation the evolution of the organism. Broth uses 96-well microtiter plate format, in which bacteria are located in a liquid growth medium which contains vary concentrations of antimicrobial agents. [28]

1.2.2 Minimum Lethal Concentration (MLC) or Minimum Bacterial Concentration (MBC)

Minimum Lethal Concentration is the lowest concentration needed to kill a specific bacterium. The MBC value is counted in agar plates, where the broth dilutions are incubated for 24h and 48h in order to observe the lowest broth dilution that inhibits growth. It is mainly used in some serious infections, when the immune system does not help in eradicating the infecting organisms, such as endocarditis or for immunosuppressed patients, but despite the fact that, their value is controversial, so the usage of the value is not widely known. [29]

The MBC is complementary to MIC and it is believed that bacterial agents are characterized as bactericidal if the MBC is no more than four times the MIC value.

1.3 Meta-analysis

Meta-analysis nowadays is at the highest scale of knowledge in science because it is a statistical combination of independent studies, having as a starting point an initial research question and as an ending point more precise estimate of the effect of the question. Most of the times the studies that are used involve random clinical trials which derive from complex points of literature, helping the researchers to find a conclusion. Meta-analysis has significant benefits because of the limitation of study size and are for sure more reliable than a single study. One important outcome is the existence of the examined effect, and the other one is to decide whether it is positive or negative.

The content of each search is important to include all the current studies because loss of them may lead to bias, as well as examination of heterogeneity is one of the most important things to take into consideration too. Apart from the fact that the language of studies is significant too, the determination of specific criteria that are clearly stated, both for acceptance and for exclusion of studies is significant. Using those criteria, next step is the evaluation of the eligibility of the studies, writing down not only those who were accepted, but also the reasons why the excluded ones were not taken into consideration. Finally, after the collection of data, the procedure of meta-analysis follows up. [30]

We performed meta-analysis using MIC values, being combined in many ways, that we are going to analyze to the next chapters. Although we thought to look after for MBC values as well, during the collection of our data, we were not able to find many values, so it is impossible to perform meta-analysis with such a small sample of values.

1.4 Purpose of this study

The purpose of this study is to investigate the antimicrobial activity of hop compounds and extracts in different microorganisms by using all the available articles from universal literature. Furthermore, through usage of meta-analysis we try to combine compounds and extracts with microorganisms in different time incubations which are available in order to find out the best antimicrobial activity and to investigate the possible benefits of hops in humans.

2 Chapter 2: Material and methods

2.1 Data collection

2.1.1 Systematic review

Systematic review, which is an analytical synthesis containing data from already published research on the topic, helped to create a clear question, topic related, in order to proceed to the meta-analysis. Systematic review has some steps, which are very important for the success and the minimization of bias and errors.

2.1.2 Creation of the question

The most important thing in these studies is the right setting of the question, which help us clarify the range of search. Due to the fact that we follow the systematic review and meta-analysis path, we should clarify our boarders through our questions, in order to search for the right published studies.

2.1.3 Clarification of research and selection criteria

In order to have a proper collection of surveys we should follow the right criteria. First of all, the preferred language was English because we want to be sure that no details will be lost during the translation. Moreover, surveys are important to be the original, in order to avoid altered ones and also the kind of survey plays a significant role. That is because abstracts, short reviews, letters or research with missed data should not be taken consider, due to the fact that we should not be able to evaluate the data.

To be more specific, due to the fact that we chose to analyze the antimicrobial activity of Humulus lupulus compounds and extracts through MIC value, we should look for studies that include this value. The compounds and extracts should also be derivatives of Humulus lupulus and not from any other plant.

2.1.4 Evaluation of research

Starting the search and evaluation, we should find our surveys in data bases which are specialized in our biomedical research field. The most known data bases are : PubMed, MEDLINE and Embase. In order to find only the ones we really need, we should create a question, which will contain all the words that describe our research topic, and connect them with the binary language bonding, which are [OR,AND,NOT]. After that,

the results, which we will receive, contain almost all surveys that we need, except of some of them which will be irrelevant with our topic.

After selecting all bibliographical searches, not only we should delete the ones which are not in our field, but also the ones that appears duplicated. As a final and most important step, we should read every article, to be able to recognize the significant information and categorize or delete them according to the criteria we selected.

2.1.5 Data register

Depending on the data which are significant for us, it is important to write them down in an Excel spreadsheet. To begin with the process, we separated the surveys including MIC and MLC, which is our main important element of research, from those who do not include these values. After the separation, the Excel spreadsheet will contain every detail we need from the article, having as first columns the PubMed ID, the authors and the year of publication. After the identification categories, there will be columns with the data we need for our meta-analysis process, like MIC value, strains and compounds. It is significant to refer to the conditions which occurred for the experiment to be done and to be more specific this includes where the strains were found, if they are Gram positive or negative, the temperature, the hours, if they are aerobic or anaerobic and finally how many times, they repeat the experiment to ensure the reliability.

2.1.6 Presentation and explanation of results

The presentation of results of this systematic analysis is shown in a PRISMA-2009 flow diagram. [31] This diagram shows the number of studies been included in this meta-analysis process after the selection criteria we referred before. At the top of the diagram, it is referred the starting number of records been identified from databases. Next step is the screening of records and the decline of studies, because we did not find MIC values in them and after that we read all of them in order to ensure that they meet the criteria, that's why we exclude some surveys too. As last step is the observation of the real number of studies included in review and also the number of individual studies included in meta-analysis. This PRISMA-2009 flow diagram is shown in the following image.

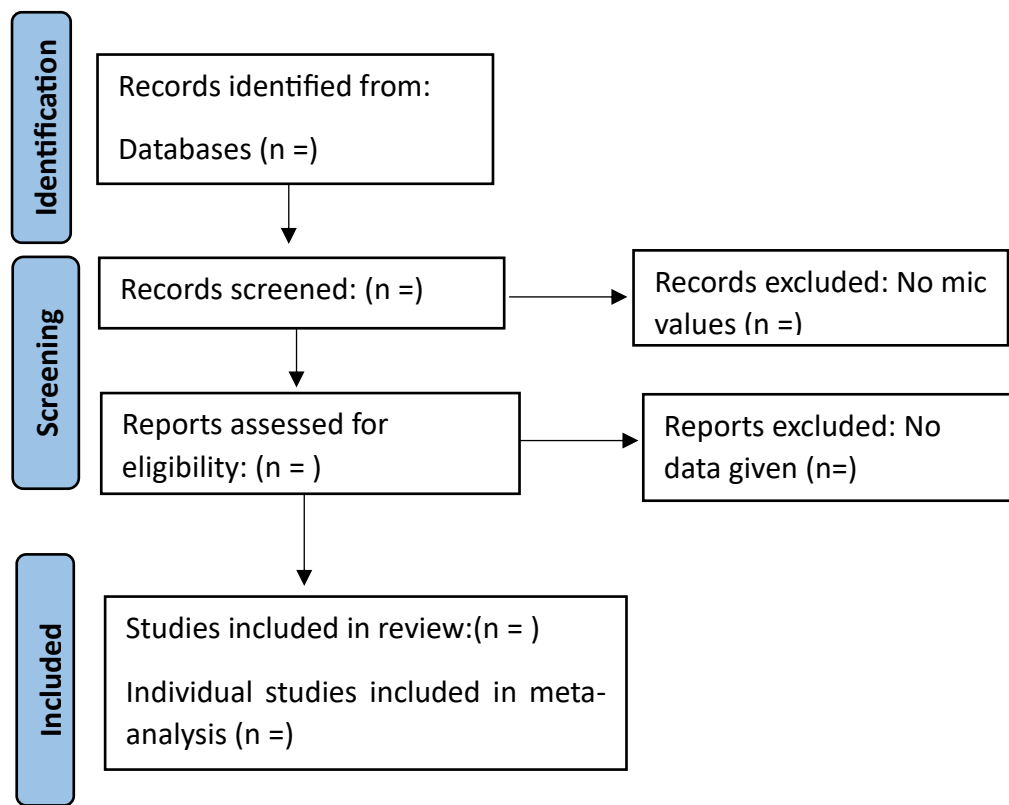


Figure 5: PRISMA-2009 flow diagram depicting steps for systematic meta-analysis.

2.2 Search strategy

The meta-analysis procedure was done, preferring reporting items for systematic reviews and meta-analysis (PRISMA) guidelines [21]. The literature search was conducted in PubMed searching the following terms: “hop antimicrobial” and (“alpha-acids” or “a-acids” or “beta-acids” or “b-acids” or adhumulone or adprehumulone or cohumulone or humulone or prehumulone or adlupulone or colupulone or lupulone or prelupulone or postlupulone or catechin or epicatechin or epigallocatechin or flavonols or kaemferol or quercetin or “multifidol glucosides” or phenolic or hydroxybenzoic or ellagic or gallic or hydroxycinnamic or caffeic or chlorogenic or ferulic or rosmarinic or prenylflavonoids or xanthohumol or isoxanthohumol or prenylnaringenin or stilbenes or piceatannol or pterostilbene or resveratrol or hydrocarbons or monoterpenes or pinene or myrcene or sesquiterpenes or humulene or caryophyllene or farnesene or linalool or “polyfunctional thiols” or mercaptohexan or thioesters or mercaptopentan or hexanethionate or desmethylxanthohumol or epicatechin or quercetin or limonene or caryophyllene or butene or humulene or “essential oils” or camphene or cymene or limonene or myrcene or ocimene or phellandrene or phellandrene or pinene or terpinene or terpinolene or thujene or acoradiene or amorphene or aromadendrene or aromadendrene or bergamotene or Bisabolene or

bisabolene or bisabolene or cadalene or cadina or cadina or cadinene or calamenene or calamene or calacorene or calarene or camphorene or camphorene or Caryophyllene or corocalene or curcumene or copaene or clovene or cubebene or elemene or elemol or farnesene or germacrene or germacatrienne or guaiane or gurjunene or humulene or muurola or muurolene or selinene or selina or ylangene or zingiberene or geraniol or linalool or geranyl or acorenol or bisabolol or cadinol or caryolanol or caryophyllene or caryophylla or cubenol or Eudesmol or eudesm or eremoligenol or farnesol or fenchy or globulol or guaial or humuladiol or humulenol or humulol or Intermedeol or junenol or muurolol or nerolidol or selin or spathulenol or viridiflorol or Bisabolol or humulene or humuladienone or humulenone or amyrin or lupeol or akazawa or Ursa or Isoprenyl or dimethoxychalcone or chalconaringenin or desmethylxanthohumol or flavokawin or methoxyflemistrictin or Humulusol or Xanthogalenol or methoxyxanthogalenol or dehydrocycloxanthohumol or Dihydroxanthohumol or methylxanthohumol or prenylxanthohumol or xanthohumol or methylnaringenin or Prenylnaringenin or diprenylnaringenin or geranylnaringenin or Munduleaflavanone or Naringenin or quercetinor or kaempferol or morin or myricetin or Astragalin or Nicotiflorin or glucopyranoside or myricetin or quercitrin or malonylglucoside or Rutin or Afzelechin or epiafzelechin or epicatechin or catechin or gallocatechin or Epigallocatechin or Procyanidin or prodelphinidin or isolariciresinol or lariciresinol or Pinoresinol or Benzoic or Hydroxybenzoic or gallic or protocatechuic or syringic or vanillic or Cinnamic or Caffeic or Cinnamic or Coumaric or ferulic or Sinapic or Chlorogenic or Cryptochlorogenic or Neochlorogenic or Coumaroylquinic or feruloylquinic or glucopyranosyl or xylopyranosyl or phloroisovalerophenone or phloroglucinol or cascadone or hulupone or hulupinic or humudifucol or humulone or humulinone or colupox or lupulone or hydroxycolupulone or deprenyllupulonol or lupuphenone or carboline or oxoindolin or oxopyrrolidine or carboxylic) and (antimicrobial or antiprotozoan OR ANTIFUNGAL OR ANTIBACTERIA OR CHEMOPREVENTION OR BIOFILM OR ANTIPARASITIC OR ANTIVIRAL)” in February 2023 and March 2023 correspondingly.

2.3 Effect size

A common value, being used in statistic, is effect size, which counts the power of the relationship between two variables. To be more specific, effect size allows us to compare values with comparable measures [32] and observe if the difference between the two variables is relevant or if it is due to change of factors. [33] In meta-analysis, the effect size combines all the studies into an overall summary. [34]. It has two categories which it can refer to, one of them is a standardized measure (odds ratio, risk ratio) and the other is the unstandardized regression (unstandardized regression coefficients).

Most of the meta-analysis processes are based on two models, fixed-effect model, or random-effect model. The first one underlies that all studies share the same effect size and the summary effect size is our common effect size. This model is used when we want to prove that all the studies included are identical and the computation of the effect size is for the identified population and not for the generalized populations. The second one assumes that the effect size is different from study to study due to the heterogeneity. On the other hand, this model is used when the studies are independent and thus, they

can not be functionally equivalent like before and also in order to generalize the results. [35]

2.3.1 Confidence interval (CI)

Confidence interval (CI) is the probability of a parameter to fall between a range of values for a proportion of time. The most common percentage is 95% and it indicates the proportion of CI that would show the true parameter if the estimate were repeated for many times. The confidence interval contains an upper and a lower bound which are calculated by this type:

$$[\text{sample statistic} - \text{margin of error}, \text{sample statistic} + \text{margin of error}]$$

There are some factors affecting the confidence interval value which are: the chosen confidence interval, the variance of the sample and the sample's size. To be more specific a large sample size leads to a shorter confidence interval because it decreases the standard error, while a higher confidence level leads to wider interval value because of the increased certainty that the parameter falls in the range. [36]

2.4 STATA

Stata is a statistical software package helping scientists to analyze and visualize the data in many fields. Stata was initially developed by Computing Resource Center in California and the first version was released in 1985. A major release in 2003 included a new graphics system and dialog boxes for all commands. Since then, a new version has been released once every two years. These graphics system was the reason why we chose to use it, because not only you can easily analyze them using commands but also make graphic designs to understand them even better. [37]

There are 4 basic commands, which were used for meta-analysis, but the most significant one 'metaan' will be explained further:

- generate: create new variable for each one in *varlist*
- sqrt(number): calculation of the square of the number inside parenthesis
- destring: convert string variables to numeric
- replace: replace string variables in *varlist* with numeric variables
- force: convert nonnumeric strings to missing values

In order the command to run properly, some mathematical symbols were used and need explanation:

Table 1	
==	Relational equality operator
!=	Relational inequality operator
	Logical operator OR
&	Logical operator AND
+	Addition symbol
-	Subtraction symbol
/	Division symbol

Table 1: Mathematical symbols for STATA command

2.4.1 metan command

In order to proceed to the meta-analysis method, we should use the command of Stata that refers to this procedure, called ‘metan’. This can help us not only combine information, to analyze them later and leading in better precision in our results but also graph the results. Metan requires either two, three, four or six variables to be declared, which are located in varlist. The syntax of ‘metan’ is:

metan varlist [if] [in] [, precalculated effect estimates options]

To the precalculated effect estimates options we use the command random, by() and label(). Random specifies random effects model using DerSimonian & Laird method, in addition to the heterogeneity being taken from the Mantel-Haenszel model. Moreover by() processing helps us separate them into subgroup, resulting in better analysis of the treatment effect between subgroups. Through label() command and especially label([namevar=namevar], [yearvar=yearvar]) we label the data by its name and year.

2.4.2 metabias command

Generally statistical bias is called the presentation of inaccurate depiction of reality, due to the collected data. The inaccuracy can occur in numerous stages, like the source of the data, the methods and the estimator. Metabias is called the difference associated with nonprocess-related factors and it is helpful when we are looking at collection of studies and not separate studies [38]. The syntax of ‘metabias’ is:

metabias moderators [if] [in] , regtest [modelopts]

We proceeded metabias analysis in our results in order to reassure their eligibility.

2.4.3 Standard Deviation (SD)

Standard Deviation (σ) is called the measure of how dispersed the data is against the mean. As higher is the SD value, far from zero value, it is an indication of scattered data and low value, that means value close to zero, indicates that the data is around the mean. [39] The formula that is used is the following:

$$SD = \sqrt{\frac{\sum (x_i - \bar{x})^2}{n - 1}}$$

Where x_i indicated each data point, μ is the mean and N total number of data points.

2.4.4 Standard Error (SE)

Standard Error (SE) is a statistic that indicates the accuracy of sample data in the population. It measures the accuracy by using standard deviation. The relationship between SE and SD is that SE is equal to SD divided by the square root of the sample size. The smaller the SE the more representative the sample will be [40]. The formula which is used is:

$$SE = \frac{\sigma}{\sqrt{n}}$$

where:

σ = The population standard deviation

$\sqrt{n}$ = The square root of the sample size

3 Results

3.1 Search strategy

In order to collect the data and proceed to meta-analysis, we used PubMed and the questions as well as the search terms was perfectly defined. The key words was: “ hop antimicrobial” and ("alpha-acids" or "a-acids" or "beta-acids" or "b-acids" or adhumulone or adprehumulone or cohumulone or humulone or prehumulone or adlupulone or colupulone or lupulone or prelupulone or postlupulone or catechin or epicatechin or epigallocatechin or flavonols or kaemferol or quercetin or "multifidol glucosides" or phenolic or hydroxybenzoic or ellagic or gallic or hydroxycinnamic or caffeic or chlorogenic or ferulic or rosmarinic or prenylflavonoids or xanthohumol or isoxanthohumol or prenylnaringenin or stilbenes or piceatannol or pterostilbene or resveratrol or hydrocarbons or monoterpenes or pinene or myrcene or sesquiterpenes or humulene or caryophyllene or farnesene or linalool or "polyfunctional thiols" or mercaptohexan or thioesters or mercaptopentan or hexanethionate or desmethylxanthohumol or epicatechin or quercetin or limonene or caryophyllene or butene or humulene or "essential oils" or camphene or cymene or limonene or myrcene or ocimene or phellandrene or phellandrene or pinene or terpinene or terpinolene or thujene or acoradiene or amorphene or aromadendrene or aromadendrene or bergamotene or Bisabolene or bisabolene or bisabolene or cadalene or cadina or cadina or cadinene or calamenene or calamene or calacorene or calarene or camphorene or camphorene or Caryophyllene or corocalene or curcumene or copaene or clovene or cubebene or elemene or elemol or farnesene or germacrene or germacatrienne or guaiane or gurjunene or humulene or muurola or muurolene or selinene or selina or ylangene or zingiberene or geraniol or linalool or geranyl or acorenol or bisabolol or cadinol or caryolanol or caryophyllene or caryophylla or cubenol or Eudesmol or eudesm or eremoligenol or farnesol or fenchy or globulol or guaial or humuladiol or humulenol or humulol or Intermedeol or junenol or muurolol or nerolidol or selin or spathulenol or viridiflorol or Bisabolol or humulene or humuladienone or humulenone or amyrin or lupeol or akazawa or Ursa or Isoprenyl or dimethoxychalcone or chalconaringenin or desmethylxanthohumol or flavokawin or methoxyflemistricin or Humulusol or Xanthogalenol or methoxyxanthogalenol or dehydrocycloxanthohumol or Dihydroxanthohumol or methylxanthohumol or prenylxanthohumol or xanthohumol or methylnaringenin or Prenylnaringenin or diprenylnaringenin or geranylnaringenin or Munduleaflavanone or Naringenin or quercetinor or kaempferol or morin or myricetin or Astragalin or Nicotiflorin or glucopyranoside or myricetin or quercitrin or malonylglucoside or Rutin or Afzelechin or epiafzelechin or epicatechin or catechin or gallocatechin or Epigallocatechin or Procyanidin or prodelphinidin or isolariciresinol or lariciresinol or Pinoresinol or Benzoic or Hydroxybenzoic or gallic or protocatechuic or syringic or vanillic or Cinnamic or Caffeic or Cinnamic or Coumaric or ferulic or Sinapic or Chlorogenic or Cryptochlorogenic or Neochlorogenic or Coumaroylquinic or feruloylquinic or glucopyranosyl or xylopyranosyl or phloroisovalerophenone or phloroglucinol or cascadone or hulupone or hulupinic or humudifucol or humulone or humulinone or

colupox or lupulone or hydroxycolupulone or deprenyllupulonol or lupuphenone or carboline or oxoindolin or oxopyrrolidine or carboxylic) and (antimicrobial or antiprotozoan OR ANTIFUNGAL OR ANTIBACTERIA OR CHEMOPREVENTION OR BIOFILM OR ANTIPARASITIC OR ANTIVIRAL)” in February 2023 and March 2023 correspondingly.

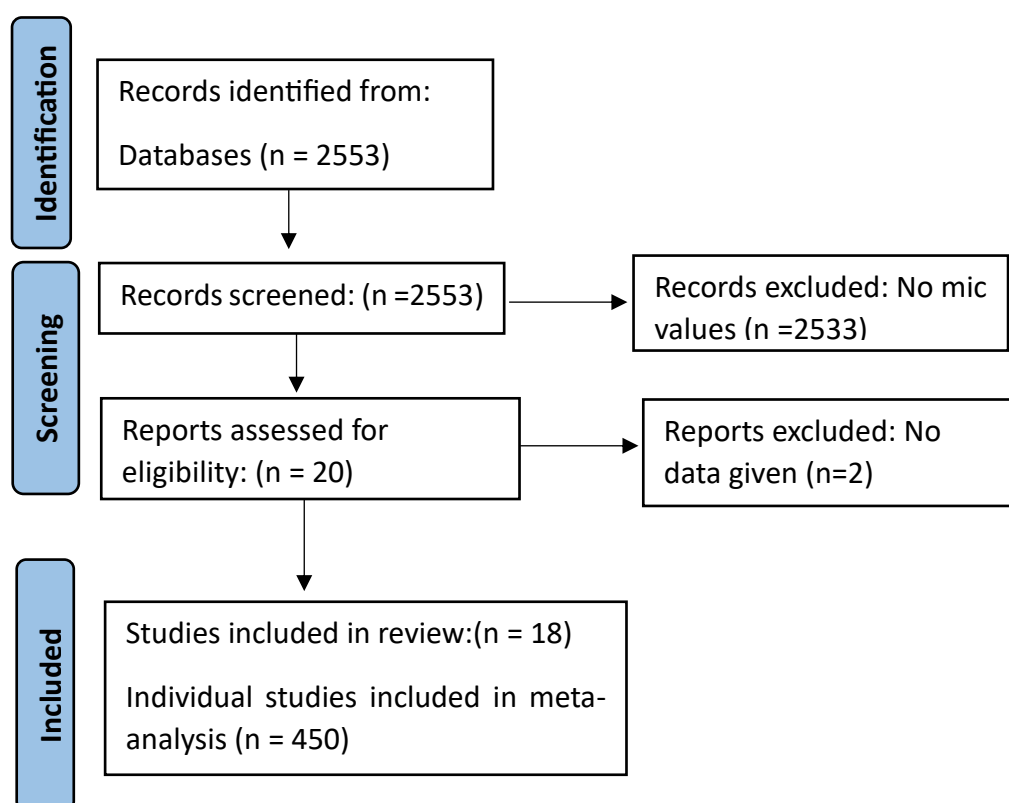


Figure 6: PRISMA-2009 flow diagram depicting steps for systematic meta-analysis.

3.2 Study selection and data extraction

While we started the first step of systematic analysis, we have in total 2553 articles, the first search term being referred above, gave us 1417 articles and the second search term with more criteria gave us 599 articles, but after duplicate criteria with the “hop antimicrobial” search term we ended up having 136 articles. Those articles were allocated in Excel spreadsheet, having as id the PMID and one more column explaining whether they have MIC values or not (YES/NO COLUMN) in order to explain why we have to eliminate some of them.

After this selection, we ended up having 20 articles with MIC values, of which the 2 have not enough data in order to be useful for meta-analysis and finally 450 reports were result of the 18 articles.

Referring to the *Humulus lupulus* compounds as well as its extracts, we counted 6 compounds and 3 extracts, while in the first category Xanthohumol has 21,55% from the whole number of reports and in the second category Hydralcoholic-extract has 17,55%.

Strains being used in this meta-analysis were counted 55, while *Clostridium difficile* has the most registers among those reports, 18,67%, being followed by *Staphylococcus aureus* with 16,67% among the whole number of strains.

Finally, among the conditions in those studies, hours of incubation are very important factor. From the 450 reports, 174 of them have 24 hours of incubation, while 276 have 48 hours.

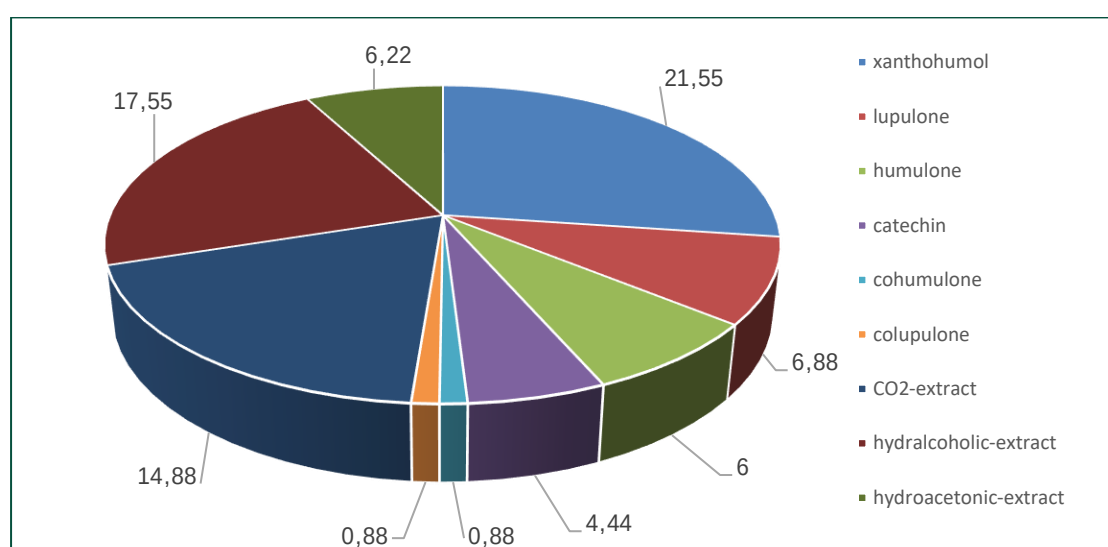


Figure 7: Pie chart illustrating hop chemical compounds and extracts.

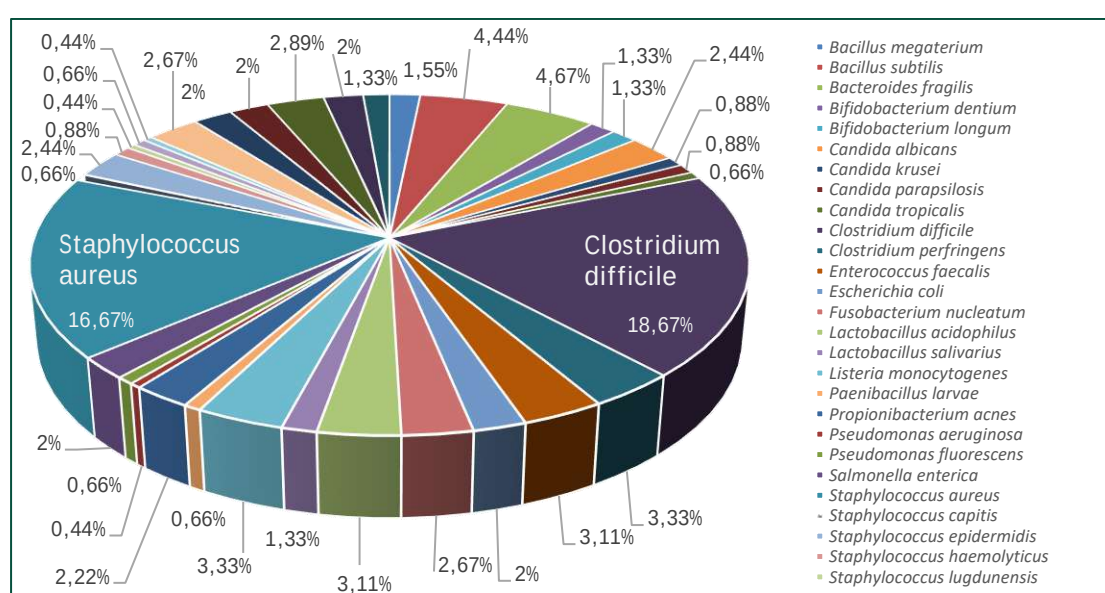


Figure 8: Pie chart illustrating microorganisms in 450 reports

3.3 Results of meta-analysis in compounds and extracts

At first, we examined the antimicrobial activity that every compounds and extracts have on microorganisms among different hours of incubation. We proceeded to meta-analysis with random effect model using STATA and the p-value: $p \leq 0.05$ in order to be statistically significant. We used the following command:

```
metan MIC stde if classcompound1 == "xanthohumol" & hours == 24 , by(strain) random label(namevar=author)
```

During meta-analysis we run the command with every possible combination like hours of incubation, compounds and extracts. Furthermore, we created three classes of compounds (classcompound1, classcompound2, classcompound3), in which we classified the compounds and extracts into wider classes, with the first one being the most specific and the latest being the most general one. We wrote down the meta-analysis results in another Excel spreadsheet and the columns were: number of studies, effect size, confidence interval, p-value and heterogeneity as well. We redid the process for by(order), by(class), by(phylum) instead of by(strain), as we chose to make a stratification of microorganisms into wider categories. Finally, we classified the strains into pathogenicity, food spoilage activity and probiotic activity and proceeded meta-analysis with this stratification too.

Strain	Pathogenicity	Food spoilage	Probiotic
Acinetobacter baumannii	opportunistic pathogens	no food spoilage	no probiotic
Aspergillus niger	opportunistic pathogens	no food spoilage	no probiotic
Bacillus amyloliquefaciens	opportunistic pathogens	no food spoilage	probiotic
Bacillus cereus	opportunistic pathogens	food spoilage	probiotic
Bacillus megaterium	opportunistic pathogens	food spoilage	probiotic
Bacillus subtilis	opportunistic pathogens	food spoilage	probiotic
Bacteroides fragilis	opportunistic pathogens	no food spoilage	probiotic
Bifidobacterium dentium	opportunistic pathogens	no food spoilage	probiotic

Bifidobacterium longum	opportunistic pathogens	no food spoilage	probiotic
Campylobacter jejuni	pathogenic	no food spoilage	no probiotic
Candida albicans	opportunistic pathogens	no food spoilage	no probiotic
Candida krusei	pathogenic	no food spoilage	no probiotic
Candida parapsilosis	opportunistic pathogens	no food spoilage	no probiotic
Candida tropicalis	pathogenic	no food spoilage	no probiotic
Clostridium difficile	opportunistic pathogens	no food spoilage	no probiotic
Clostridium perfringens	opportunistic pathogens	food spoilage	no probiotic
Corynebacterium	opportunistic pathogens	no food spoilage	no probiotic
Eikenella corrodens	opportunistic pathogens	no food spoilage	no probiotic
Enterococcus faecalis	opportunistic pathogens	no food spoilage	no probiotic
Enterococcus sp.	pathogenic	no food spoilage	no probiotic
Escherichia coli	opportunistic pathogens	food spoilage	no probiotic
Fusobacterium nucleatum	opportunistic pathogens	no food spoilage	no probiotic
Lactobacillus acidophilus	opportunistic pathogens	food spoilage	probiotic
Lactobacillus fermentum	opportunistic pathogens	food spoilage	probiotic
Lactobacillus plantarum	opportunistic pathogens	no food spoilage	probiotic
Lactobacillus salivarius	opportunistic pathogens	food spoilage	probiotic
Lactococcus lactis	opportunistic pathogens	no food spoilage	probiotic
Leuconostoc mesenteroides	pathogenic	no food spoilage	probiotic
Listeria monocytogenes	opportunistic pathogens	food spoilage	no probiotic
Mucor plumbeus	opportunistic pathogens	no food spoilage	no probiotic
Mycobacterium smegmatis	opportunistic pathogens	no food spoilage	no probiotic

Mycobacterium tuberculosis	opportunistic pathogens	food spoilage	no probiotic
Paenibacillus larvae	opportunistic pathogens	no food spoilage	no probiotic
Pediococcus acidilactici	opportunistic pathogens	no food spoilage	no probiotic
Penicillium spp	opportunistic pathogens	no food spoilage	no probiotic
Propionibacterium acnes	opportunistic pathogens	no food spoilage	no probiotic
Pseudomonas aeruginosa	opportunistic pathogens	no food spoilage	no probiotic
Pseudomonas fluorescens	opportunistic pathogens	no food spoilage	no probiotic
Saccharomyces cerevisiae	opportunistic pathogens	no food spoilage	probiotic
Salmonella enterica	pathogenic	food spoilage	no probiotic
Staphylococcus aureus	opportunistic pathogens	food spoilage	no probiotic
Staphylococcus capitis	opportunistic pathogens	no food spoilage	no probiotic
Staphylococcus epidermidis	opportunistic pathogens	no food spoilage	no probiotic
Staphylococcus haemolyticus	opportunistic pathogens	no food spoilage	no probiotic
Staphylococcus lugdunensis	opportunistic pathogens	no food spoilage	no probiotic
Staphylococcus warneri	opportunistic pathogens	no food spoilage	no probiotic
Stenotrophomonas maltophilia	opportunistic pathogens	no food spoilage	no probiotic
Streptococcus agalactiae	opportunistic pathogens	food spoilage	no probiotic
Streptococcus aureus	opportunistic pathogens	food spoilage	no probiotic
Streptococcus dysgalactiae	opportunistic pathogens	food spoilage	no probiotic
Streptococcus mutans	opportunistic pathogens	food spoilage	no probiotic
Streptococcus salivarius	opportunistic pathogens	food spoilage	no probiotic
Streptococcus sanguinis	opportunistic pathogens	food spoilage	no probiotic

Streptococcus saprophyticus	opportunistic pathogens	food spoilage	no probiotic
Streptococcus sobrinus	opportunistic pathogens	food spoilage	no probiotic

Table 2: Table showing the division of microorganisms into pathogenic, probiotic, food-spoilage.

Hop compounds	Hop extracts
catechin	CO2-extract
cohumulone	hydraulic-holistic-extract
colupulone	hydroacetic-extract
humulone	
lupulone	
xanthohumol	

Table 3: Table showing division of compounds and extracts.

As we referred before, we divided the compounds into three categories classcompound, classcompound2, classcompound3.

Here we present the compounds of classcompound1:

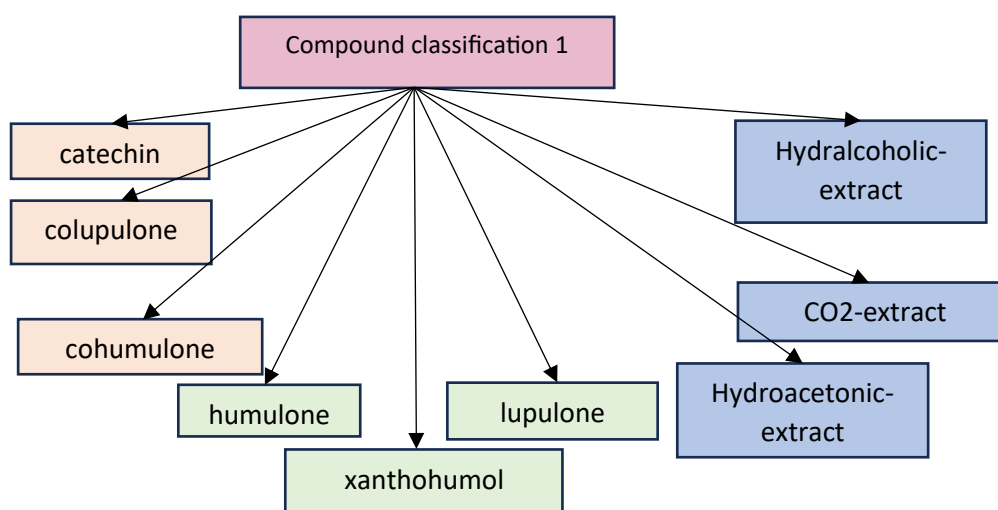


Figure 9: Graph showing compound classification 1.

Classcompound2 includes wider categories of compounds and extracts, being presented

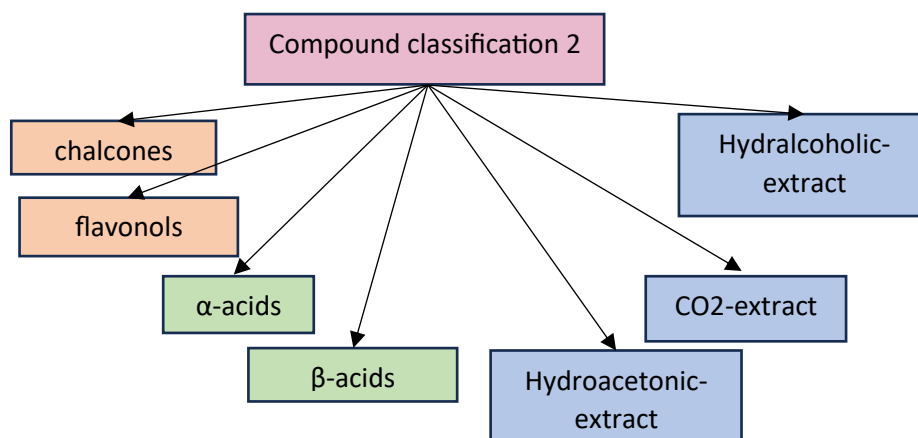


Figure 10: Graph showing compound classification 2.

Classcompound3 includes the widest possible categories of those compounds:

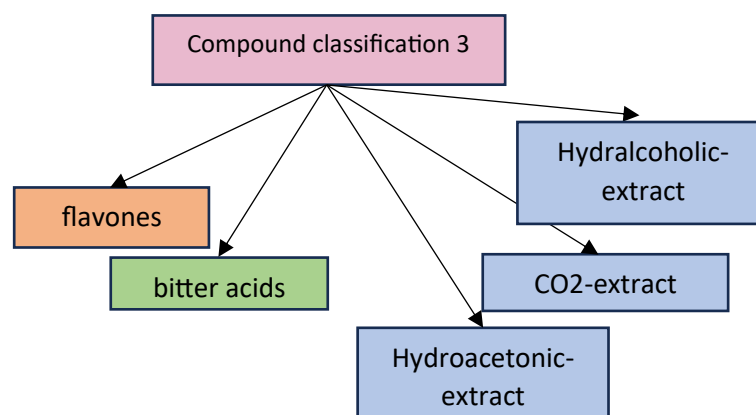


Figure 11: Graph showing compound classification 3

PMID	Year	Author	MIC	Units(μ g/mL)	Strain	Order	Class	Phylum	Classcompound1	Classcompound2	Classcompound3	Hours	Number of experiments
25494620	2015	B Kramer	6.1	μ g/mL	Staphylococcus aureus	Bacillales	Bacilli	Bacillota	xanthohumol	chalcones	flavonoids	48	4
			3.1	μ g/mL	Staphylococcus aureus	Bacillales	Bacilli	Bacillota	xanthohumol	chalcones	flavonoids	48	4
			6.3	μ g/mL	Staphylococcus aureus	Bacillales	Bacilli	Bacillota	xanthohumol	chalcones	flavonoids	48	4
			200	μ g/mL	Staphylococcus aureus	Bacillales	Bacilli	Bacillota	CO2-extract	CO2-extract	CO2-extract	48	4
			25	μ g/mL	Staphylococcus aureus	Bacillales	Bacilli	Bacillota	CO2-extract	CO2-extract	CO2-extract	48	4
			25	μ g/mL	Staphylococcus aureus	Bacillales	Bacilli	Bacillota	CO2-extract	CO2-extract	CO2-extract	48	4
			6.3	μ g/mL	Staphylococcus aureus	Bacillales	Bacilli	Bacillota	CO2-extract	CO2-extract	CO2-extract	48	4
			1.6	μ g/mL	Staphylococcus aureus	Bacillales	Bacilli	Bacillota	CO2-extract	CO2-extract	CO2-extract	48	4
			3.1	μ g/mL	Staphylococcus aureus	Bacillales	Bacilli	Bacillota	CO2-extract	CO2-extract	CO2-extract	48	4
			12.5	μ g/mL	Listeria monocytogenes	Bacillales	Bacilli	Bacillota	xanthohumol	chalcones	flavonoids	48	4
			3.1	μ g/mL	Listeria monocytogenes	Bacillales	Bacilli	Bacillota	xanthohumol	chalcones	flavonoids	48	4
			3.1	μ g/mL	Listeria monocytogenes	Bacillales	Bacilli	Bacillota	xanthohumol	chalcones	flavonoids	48	4
			200	μ g/mL	Listeria monocytogenes	Bacillales	Bacilli	Bacillota	CO2-extract	CO2-extract	CO2-extract	48	4
			6.3	μ g/mL	Listeria monocytogenes	Bacillales	Bacilli	Bacillota	CO2-extract	CO2-extract	CO2-extract	48	4
			6.3	μ g/mL	Listeria monocytogenes	Bacillales	Bacilli	Bacillota	CO2-extract	CO2-extract	CO2-extract	48	4
			12.5	μ g/mL	Listeria monocytogenes	Bacillales	Bacilli	Bacillota	CO2-extract	CO2-extract	CO2-extract	48	4
			1.6	μ g/mL	Listeria monocytogenes	Bacillales	Bacilli	Bacillota	CO2-extract	CO2-extract	CO2-extract	48	4
			1.6	μ g/mL	Listeria monocytogenes	Bacillales	Bacilli	Bacillota	CO2-extract	CO2-extract	CO2-extract	48	4
			200	μ g/mL	Escherichia coli	Enterobacterales	Gamma proteobacteria	Pseudomonadota	xanthohumol	chalcones	flavonoids	48	4
			200	μ g/mL	Escherichia coli	Enterobacterales	Gamma proteobacteria	Pseudomonadota	xanthohumol	chalcones	flavonoids	48	4
			200	μ g/mL	Escherichia coli	Enterobacterales	Gamma proteobacteria	Pseudomonadota	xanthohumol	chalcones	flavonoids	48	4
			5000	μ g/mL	Escherichia coli	Enterobacterales	Gamma proteobacteria	Pseudomonadota	CO2-extract	CO2-extract	CO2-extract	48	4
			2500	μ g/mL	Escherichia coli	Enterobacterales	Gamma proteobacteria	Pseudomonadota	CO2-extract	CO2-extract	CO2-extract	48	4
			1250	μ g/mL	Escherichia coli	Enterobacterales	Gamma proteobacteria	Pseudomonadota	CO2-extract	CO2-extract	CO2-extract	48	4
			5000	μ g/mL	Escherichia coli	Enterobacterales	Gamma proteobacteria	Pseudomonadota	CO2-extract	CO2-extract	CO2-extract	48	4
			1250	μ g/mL	Escherichia coli	Enterobacterales	Gamma proteobacteria	Pseudomonadota	CO2-extract	CO2-extract	CO2-extract	48	4
			625	μ g/mL	Escherichia coli	Enterobacterales	Gamma proteobacteria	Pseudomonadota	CO2-extract	CO2-extract	CO2-extract	48	4
			200	μ g/mL	Salmonella enterica	Enterobacterales	Gamma proteobacteria	Pseudomonadota	xanthohumol	chalcones	flavonoids	48	4
			200	μ g/mL	Salmonella enterica	Enterobacterales	Gamma proteobacteria	Pseudomonadota	xanthohumol	chalcones	flavonoids	48	4
			200	μ g/mL	Salmonella enterica	Enterobacterales	Gamma proteobacteria	Pseudomonadota	xanthohumol	chalcones	flavonoids	48	4

			5000	µg/mL	Salmonella enterica	Enterobacterales	Gamma proteobacteria	Pseudomonadota	CO2-extract	CO2-extract	CO2-extract	48	4
			2500	µg/mL	Salmonella enterica	Enterobacterales	Gamma proteobacteria	Pseudomonadota	CO2-extract	CO2-extract	CO2-extract	48	4
			1250	µg/mL	Salmonella enterica	Enterobacterales	Gamma proteobacteria	Pseudomonadota	CO2-extract	CO2-extract	CO2-extract	48	4
			5000	µg/mL	Salmonella enterica	Enterobacterales	Gamma proteobacteria	Pseudomonadota	CO2-extract	CO2-extract	CO2-extract	48	4
			1250	µg/mL	Salmonella enterica	Enterobacterales	Gamma proteobacteria	Pseudomonadota	CO2-extract	CO2-extract	CO2-extract	48	4
			625	µg/mL	Salmonella enterica	Enterobacterales	Gamma proteobacteria	Pseudomonadota	CO2-extract	CO2-extract	CO2-extract	48	4
30634461	2019	Natalja Weber	3.1	µg/mL	Propionibacterium acnes	Propionibacteriales	Actinomycetia	Actinomycetota	CO2-extract	CO2-extract	CO2-extract	24	3
			4,65	µg/mL	Propionibacterium acnes	Propionibacteriales	Actinomycetia	Actinomycetota	CO2-extract	CO2-extract	CO2-extract	24	3
			3.1	µg/mL	Propionibacterium acnes	Propionibacteriales	Actinomycetia	Actinomycetota	CO2-extract	CO2-extract	CO2-extract	24	3
			3.1	µg/mL	Propionibacterium acnes	Propionibacteriales	Actinomycetia	Actinomycetota	CO2-extract	CO2-extract	CO2-extract	24	3
			9,375	µg/mL	Staphylococcus aureus	Bacillales	Bacilli	Bacillota	CO2-extract	CO2-extract	CO2-extract	24	3
			9,375	µg/mL	Staphylococcus aureus	Bacillales	Bacilli	Bacillota	CO2-extract	CO2-extract	CO2-extract	24	3
			6.25	µg/mL	Staphylococcus aureus	Bacillales	Bacilli	Bacillota	CO2-extract	CO2-extract	CO2-extract	24	3
			12.5	µg/mL	Staphylococcus aureus	Bacillales	Bacilli	Bacillota	CO2-extract	CO2-extract	CO2-extract	24	3
			160	µg/mL	Bacteroides fragilis	Bacteroidales	Bacteroidia	Bacteroida		α-acids	bitter acids	48	4
			680	µg/mL	Bacteroides fragilis	Bacteroidales	Bacteroidia	Bacteroida		α-acids	bitter acids	48	4
			900	µg/mL	Bacteroides fragilis	Bacteroidales	Bacteroidia	Bacteroida		α-acids	bitter acids	48	4
			1540	µg/mL	Bacteroides fragilis	Bacteroidales	Bacteroidia	Bacteroida		α-acids	bitter acids	48	4
			1150	µg/mL	Bacteroides fragilis	Bacteroidales	Bacteroidia	Bacteroida		α-acids	bitter acids	48	4
			260	µg/mL	Bacteroides fragilis	Bacteroidales	Bacteroidia	Bacteroida		α-acids	bitter acids	48	4
			680	µg/mL	Bacteroides fragilis	Bacteroidales	Bacteroidia	Bacteroida		α-acids	bitter acids	48	4
			840	µg/mL	Clostridium perfringens	Eubacteriales	Clostridia	Bacillota		α-acids	bitter acids	48	4
			1370	µg/mL	Clostridium perfringens	Eubacteriales	Clostridia	Bacillota		α-acids	bitter acids	48	4
			1190	µg/mL	Clostridium perfringens	Eubacteriales	Clostridia	Bacillota		α-acids	bitter acids	48	4
			680	µg/mL	Clostridium perfringens	Eubacteriales	Clostridia	Bacillota		α-acids	bitter acids	48	4
			1230	µg/mL	Clostridium perfringens	Eubacteriales	Clostridia	Bacillota		α-acids	bitter acids	48	4
			320	µg/mL	Clostridium difficile	Eubacteriales	Clostridia	Bacillota		α-acids	bitter acids	48	4
			770	µg/mL	Clostridium difficile	Eubacteriales	Clostridia	Bacillota		α-acids	bitter acids	48	4
			510	µg/mL	Clostridium difficile	Eubacteriales	Clostridia	Bacillota		α-acids	bitter acids	48	4

			510	µg/mL	Clostridium difficile	Eubacteriales	Clostridia	Bacillota		α-acids	bitter acids	48	4
			580	µg/mL	Clostridium difficile	Eubacteriales	Clostridia	Bacillota		α-acids	bitter acids	48	4
			770	µg/mL	Clostridium difficile	Eubacteriales	Clostridia	Bacillota		α-acids	bitter acids	48	4
			1020	µg/mL	Clostridium difficile	Eubacteriales	Clostridia	Bacillota		α-acids	bitter acids	48	4
			510	µg/mL	Clostridium difficile	Eubacteriales	Clostridia	Bacillota		α-acids	bitter acids	48	4
			510	µg/mL	Clostridium difficile	Eubacteriales	Clostridia	Bacillota		α-acids	bitter acids	48	4
			340	µg/mL	Clostridium difficile	Eubacteriales	Clostridia	Bacillota		α-acids	bitter acids	48	4
			640	µg/mL	Clostridium difficile	Eubacteriales	Clostridia	Bacillota		α-acids	bitter acids	48	4
			1020	µg/mL	Clostridium difficile	Eubacteriales	Clostridia	Bacillota		α-acids	bitter acids	48	4
			1020	µg/mL	Clostridium difficile	Eubacteriales	Clostridia	Bacillota		α-acids	bitter acids	48	4
			430	µg/mL	Clostridium difficile	Eubacteriales	Clostridia	Bacillota		α-acids	bitter acids	48	4
			340	µg/mL	Clostridium difficile	Eubacteriales	Clostridia	Bacillota		α-acids	bitter acids	48	4
			680	µg/mL	Clostridium difficile	Eubacteriales	Clostridia	Bacillota		α-acids	bitter acids	48	4
			2040	µg/mL	Clostridium difficile	Eubacteriales	Clostridia	Bacillota		α-acids	bitter acids	48	4
			510	µg/mL	Clostridium difficile	Eubacteriales	Clostridia	Bacillota		α-acids	bitter acids	48	4
			300	µg/mL	Clostridium difficile	Eubacteriales	Clostridia	Bacillota		α-acids	bitter acids	48	4
			680	µg/mL	Clostridium difficile	Eubacteriales	Clostridia	Bacillota		α-acids	bitter acids	48	4
			510	µg/mL	Clostridium difficile	Eubacteriales	Clostridia	Bacillota		α-acids	bitter acids	48	4
			1020	µg/mL	Clostridium difficile	Eubacteriales	Clostridia	Bacillota		α-acids	bitter acids	48	4
			850	µg/mL	Clostridium difficile	Eubacteriales	Clostridia	Bacillota		α-acids	bitter acids	48	4
			1020	µg/mL	Clostridium difficile	Eubacteriales	Clostridia	Bacillota		α-acids	bitter acids	48	4
			680	µg/mL	Clostridium difficile	Eubacteriales	Clostridia	Bacillota		α-acids	bitter acids	48	4
			1020	µg/mL	Clostridium difficile	Eubacteriales	Clostridia	Bacillota		α-acids	bitter acids	48	4
			1020	µg/mL	Clostridium difficile	Eubacteriales	Clostridia	Bacillota		α-acids	bitter acids	48	4
			1020	µg/mL	Clostridium difficile	Eubacteriales	Clostridia	Bacillota		α-acids	bitter acids	48	4
			190	µg/mL	Bacteroides fragilis	Bacteroidales	Bacteroidia	Bacteroida		β-acids	bitter acids	48	4
			340	µg/mL	Bacteroides fragilis	Bacteroidales	Bacteroidia	Bacteroida		β-acids	bitter acids	48	4
			320	µg/mL	Bacteroides fragilis	Bacteroidales	Bacteroidia	Bacteroida		β-acids	bitter acids	48	4
			430	µg/mL	Bacteroides fragilis	Bacteroidales	Bacteroidia	Bacteroida		β-acids	bitter acids	48	4
			260	µg/mL	Bacteroides fragilis	Bacteroidales	Bacteroidia	Bacteroida		β-acids	bitter acids	48	4
			220	µg/mL	Bacteroides fragilis	Bacteroidales	Bacteroidia	Bacteroida		β-acids	bitter acids	48	4
			50	µg/mL	Bacteroides fragilis	Bacteroidales	Bacteroidia	Bacteroida		β-acids	bitter acids	48	4
			170	µg/mL	Clostridium perfringens	Eubacteriales	Clostridia	Bacillota		β-acids	bitter acids	48	4
			210	µg/mL	Clostridium perfringens	Eubacteriales	Clostridia	Bacillota		β-acids	bitter acids	48	4

289604 74	2017	Pavel Cermak	260	µg/mL	Clostridium perfringens	Eubacter iales	Clostridi a	Bacillota		β-acids	bitter acids	48	4
			200	µg/mL	Clostridium perfringens	Eubacter iales	Clostridi a	Bacillota		β-acids	bitter acids	48	4
			150	µg/mL	Clostridium perfringens	Eubacter iales	Clostridi a	Bacillota		β-acids	bitter acids	48	4
			24	µg/mL	Clostridium difficile	Eubacter iales	Clostridi a	Bacillota		β-acids	bitter acids	48	4
			80	µg/mL	Clostridium difficile	Eubacter iales	Clostridi a	Bacillota		β-acids	bitter acids	48	4
			48	µg/mL	Clostridium difficile	Eubacter iales	Clostridi a	Bacillota		β-acids	bitter acids	48	4
			21	µg/mL	Clostridium difficile	Eubacter iales	Clostridi a	Bacillota		β-acids	bitter acids	48	4
			72	µg/mL	Clostridium difficile	Eubacter iales	Clostridi a	Bacillota		β-acids	bitter acids	48	4
			21	µg/mL	Clostridium difficile	Eubacter iales	Clostridi a	Bacillota		β-acids	bitter acids	48	4
			68	µg/mL	Clostridium difficile	Eubacter iales	Clostridi a	Bacillota		β-acids	bitter acids	48	4
			32	µg/mL	Clostridium difficile	Eubacter iales	Clostridi a	Bacillota		β-acids	bitter acids	48	4
			21	µg/mL	Clostridium difficile	Eubacter iales	Clostridi a	Bacillota		β-acids	bitter acids	48	4
			27	µg/mL	Clostridium difficile	Eubacter iales	Clostridi a	Bacillota		β-acids	bitter acids	48	4
			36	µg/mL	Clostridium difficile	Eubacter iales	Clostridi a	Bacillota		β-acids	bitter acids	48	4
			96	µg/mL	Clostridium difficile	Eubacter iales	Clostridi a	Bacillota		β-acids	bitter acids	48	4
			40	µg/mL	Clostridium difficile	Eubacter iales	Clostridi a	Bacillota		β-acids	bitter acids	48	4
			80	µg/mL	Clostridium difficile	Eubacter iales	Clostridi a	Bacillota		β-acids	bitter acids	48	4
			19	µg/mL	Clostridium difficile	Eubacter iales	Clostridi a	Bacillota		β-acids	bitter acids	48	4
			27	µg/mL	Clostridium difficile	Eubacter iales	Clostridi a	Bacillota		β-acids	bitter acids	48	4
			43	µg/mL	Clostridium difficile	Eubacter iales	Clostridi a	Bacillota		β-acids	bitter acids	48	4
			27	µg/mL	Clostridium difficile	Eubacter iales	Clostridi a	Bacillota		β-acids	bitter acids	48	4
			9	µg/mL	Clostridium difficile	Eubacter iales	Clostridi a	Bacillota		β-acids	bitter acids	48	4
			24	µg/mL	Clostridium difficile	Eubacter iales	Clostridi a	Bacillota		β-acids	bitter acids	48	4
			12	µg/mL	Clostridium difficile	Eubacter iales	Clostridi a	Bacillota		β-acids	bitter acids	48	4
			53	µg/mL	Clostridium difficile	Eubacter iales	Clostridi a	Bacillota		β-acids	bitter acids	48	4
			48	µg/mL	Clostridium difficile	Eubacter iales	Clostridi a	Bacillota		β-acids	bitter acids	48	4
			24	µg/mL	Clostridium difficile	Eubacter iales	Clostridi a	Bacillota		β-acids	bitter acids	48	4
			12	µg/mL	Clostridium difficile	Eubacter iales	Clostridi a	Bacillota		β-acids	bitter acids	48	4
			48	µg/mL	Clostridium difficile	Eubacter iales	Clostridi a	Bacillota		β-acids	bitter acids	48	4
			28	µg/mL	Clostridium difficile	Eubacter iales	Clostridi a	Bacillota		β-acids	bitter acids	48	4
			48	µg/mL	Clostridium difficile	Eubacter iales	Clostridi a	Bacillota		β-acids	bitter acids	48	4
			15	µg/mL	Bacteroides fragilis	Bacteroi dales	Bacteroi dia	Bacteroid a	xanthohumol	chalcones	flavonoids	48	4
			56	µg/mL	Bacteroides fragilis	Bacteroi dales	Bacteroi dia	Bacteroid a	xanthohumol	chalcones	flavonoids	48	4
			29	µg/mL	Bacteroides fragilis	Bacteroi dales	Bacteroi dia	Bacteroid a	xanthohumol	chalcones	flavonoids	48	4

[illegible]

			64	µg/mL	Clostridium difficile	Eubacteriales	Clostridia	Bacillota	xanthohumol	chalcones	flavonoids	48	4
			64	µg/mL	Clostridium difficile	Eubacteriales	Clostridia	Bacillota	xanthohumol	chalcones	flavonoids	48	4
			53	µg/mL	Clostridium difficile	Eubacteriales	Clostridia	Bacillota	xanthohumol	chalcones	flavonoids	48	4
29407045	2018	Katerina Bogdanova	7.5	µg/mL	Staphylococcus epidermidis	Bacillales	Bacilli	Bacillota	humulone	α-acids	bitter acids	24	3
			30	µg/mL	Staphylococcus epidermidis	Bacillales	Bacilli	Bacillota	humulone	α-acids	bitter acids	24	3
			15	µg/mL	Staphylococcus capitis	Bacillales	Bacilli	Bacillota	humulone	α-acids	bitter acids	24	3
			15	µg/mL	Staphylococcus aureus	Bacillales	Bacilli	Bacillota	humulone	α-acids	bitter acids	24	3
			15	µg/mL	Staphylococcus aureus	Bacillales	Bacilli	Bacillota	humulone	α-acids	bitter acids	24	3
			0.5	µg/mL	Staphylococcus epidermidis	Bacillales	Bacilli	Bacillota	lupulone	β-acids	bitter acids	24	3
			4	µg/mL	Staphylococcus epidermidis	Bacillales	Bacilli	Bacillota	lupulone	β-acids	bitter acids	24	3
			0.5	µg/mL	Staphylococcus capitis	Bacillales	Bacilli	Bacillota	lupulone	β-acids	bitter acids	24	3
			0.5	µg/mL	Staphylococcus aureus	Bacillales	Bacilli	Bacillota	lupulone	β-acids	bitter acids	24	3
			0.5	µg/mL	Staphylococcus aureus	Bacillales	Bacilli	Bacillota	lupulone	β-acids	bitter acids	24	3
			2	µg/mL	Staphylococcus epidermidis	Bacillales	Bacilli	Bacillota	xanthohumol	chalcones	flavonoids	24	3
			2	µg/mL	Staphylococcus epidermidis	Bacillales	Bacilli	Bacillota	xanthohumol	chalcones	flavonoids	24	3
			2	µg/mL	Staphylococcus capitis	Bacillales	Bacilli	Bacillota	xanthohumol	chalcones	flavonoids	24	3
			2	µg/mL	Staphylococcus aureus	Bacillales	Bacilli	Bacillota	xanthohumol	chalcones	flavonoids	24	3
			4	µg/mL	Staphylococcus aureus	Bacillales	Bacilli	Bacillota	xanthohumol	chalcones	flavonoids	24	3
8930705	1996	Ann E. Larsona	300	µg/mL	Listeria monocytogenes	Bacillales	Bacilli	Bacillota	CO2-extract	CO2-extract	CO2-extract	24	4
			300	µg/mL	Listeria monocytogenes	Bacillales	Bacilli	Bacillota	CO2-extract	CO2-extract	CO2-extract	24	4
			10	µg/mL	Listeria monocytogenes	Bacillales	Bacilli	Bacillota	CO2-extract	CO2-extract	CO2-extract	24	4
			10	µg/mL	Listeria monocytogenes	Bacillales	Bacilli	Bacillota	CO2-extract	CO2-extract	CO2-extract	24	4
			0.195	µg/mL	Staphylococcus aureus	Bacillales	Bacilli	Bacillota	CO2-extract	CO2-extract	CO2-extract	24	3
			0.195	µg/mL	Staphylococcus aureus	Bacillales	Bacilli	Bacillota	xanthohumol	chalcones	flavonoids	24	3
			0.098	µg/mL	Staphylococcus epidermidis	Bacillales	Bacilli	Bacillota	CO2-extract	CO2-extract	CO2-extract	24	3
			0.098	µg/mL	Staphylococcus epidermidis	Bacillales	Bacilli	Bacillota	xanthohumol	chalcones	flavonoids	24	3
			0.391	µg/mL	Streptococcus mutans	Lactobacillales	Bacilli	Bacillota	CO2-extract	CO2-extract	CO2-extract	48	3
			0.391	µg/mL	Streptococcus mutans	Lactobacillales	Bacilli	Bacillota	xanthohumol	chalcones	flavonoids	48	3
			0.781	µg/mL	Streptococcus sanguinis	Lactobacillales	Bacilli	Bacillota	CO2-extract	CO2-extract	CO2-extract	48	3
			0.781	µg/mL	Streptococcus sanguinis	Lactobacillales	Bacilli	Bacillota	xanthohumol	chalcones	flavonoids	48	3

33921703	2021	Katarzy na Klimek	15,6 25	µg/mL	Propionibacterium acnes	Propionibacteriales	Actinomycetia	Actinomycetota	CO2-extract	CO2-extract	CO2-extract	48	3
			62.5	µg/mL	Propionibacterium acnes	Propionibacteriales	Actinomycetia	Actinomycetota	xanthohumol	chalcones	flavonoids	48	3
			15,6 25	µg/mL	Propionibacterium acnes	Propionibacteriales	Actinomycetia	Actinomycetota	CO2-extract	CO2-extract	CO2-extract	48	3
			31.2 5	µg/mL	Propionibacterium acnes	Propionibacteriales	Actinomycetia	Actinomycetota	xanthohumol	chalcones	flavonoids	48	3
			0.19 5	µg/mL	Staphylococcus aureus	Bacillales	Bacilli	Bacillota	CO2-extract	CO2-extract	CO2-extract	24	3
			0.09 8	µg/mL	Staphylococcus epidermidis	Bacillales	Bacilli	Bacillota	CO2-extract	CO2-extract	CO2-extract	24	3
			0.39 1	µg/mL	Streptococcus mutans	Lactobacillales	Bacilli	Bacillota	CO2-extract	CO2-extract	CO2-extract	48	3
			0.78 1	µg/mL	Streptococcus sanguinis	Lactobacillales	Bacilli	Bacillota	CO2-extract	CO2-extract	CO2-extract	48	3
			15,6 25	µg/mL	Propionibacterium acnes	Propionibacteriales	Actinomycetia	Actinomycetota	CO2-extract	CO2-extract	CO2-extract	48	3
			15,6 25	µg/mL	Propionibacterium acnes	Propionibacteriales	Actinomycetia	Actinomycetota	CO2-extract	CO2-extract	CO2-extract	48	3
			39	µg/mL	Corynebacterium	Mycobacteriales	Actinomycetia	Actinomycetota	hydralcoholic-extract	hydralcoholic-extract	hydralcoholic-extract	24	3
			39	µg/mL	Enterococcus faecalis	Lactobacillales	Bacilli	Bacillota	hydralcoholic-extract	hydralcoholic-extract	hydralcoholic-extract	24	3
			156	µg/mL	Enterococcus sp.	Lactobacillales	Bacilli	Bacillota	hydralcoholic-extract	hydralcoholic-extract	hydralcoholic-extract	24	3
			39	µg/mL	Mycobacterium smegmatis	Mycobacteriales	Actinomycetia	Actinomycetota	hydralcoholic-extract	hydralcoholic-extract	hydralcoholic-extract	24	3
			39	µg/mL	Staphylococcus aureus	Bacillales	Bacilli	Bacillota	hydralcoholic-extract	hydralcoholic-extract	hydralcoholic-extract	24	3
			39	µg/mL	Staphylococcus aureus	Bacillales	Bacilli	Bacillota	hydralcoholic-extract	hydralcoholic-extract	hydralcoholic-extract	24	3
			39	µg/mL	Staphylococcus epidermidis	Bacillales	Bacilli	Bacillota	hydralcoholic-extract	hydralcoholic-extract	hydralcoholic-extract	24	3
			98	µg/mL	Staphylococcus epidermidis	Bacillales	Bacilli	Bacillota	hydralcoholic-extract	hydralcoholic-extract	hydralcoholic-extract	24	3
			156	µg/mL	Staphylococcus lugdunensis	Bacillales	Bacilli	Bacillota	hydralcoholic-extract	hydralcoholic-extract	hydralcoholic-extract	24	3
			39	µg/mL	Staphylococcus warneri	Bacillales	Bacilli	Bacillota	hydralcoholic-extract	hydralcoholic-extract	hydralcoholic-extract	24	3
			39	µg/mL	Streptococcus agalactiae	Lactobacillales	Bacilli	Bacillota	hydralcoholic-extract	hydralcoholic-extract	hydralcoholic-extract	24	3
			78	µg/mL	Streptococcus agalactiae	Lactobacillales	Bacilli	Bacillota	hydralcoholic-extract	hydralcoholic-extract	hydralcoholic-extract	24	3
			39	µg/mL	Streptococcus dysgalactiae	Lactobacillales	Bacilli	Bacillota	hydralcoholic-extract	hydralcoholic-extract	hydralcoholic-extract	24	3
			625	µg/mL	Staphylococcus lugdunensis	Bacillales	Bacilli	Bacillota	hydralcoholic-extract	hydralcoholic-extract	hydralcoholic-extract	24	3
			625	µg/mL	Staphylococcus warneri	Bacillales	Bacilli	Bacillota	hydralcoholic-extract	hydralcoholic-extract	hydralcoholic-extract	24	3

308758 54	2019	Laetitia Bocquet	625	µg/mL	Acinetobacter baumannii	Pseudom onadales	Gamma proteob acteria	Pseudom onadota	hydralcoholic -extract	hydralcohol ic-extract	hydralcohol ic-extract	24	3
			625	µg/mL	Pseudomonas aeruginosa	Pseudom onadales	Gamma proteob acteria	Pseudom onadota	hydralcoholic -extract	hydralcohol ic-extract	hydralcohol ic-extract	24	3
			625	µg/mL	Pseudomonas aeruginosa	Pseudom onadales	Gamma proteob acteria	Pseudom onadota	hydralcoholic -extract	hydralcohol ic-extract	hydralcohol ic-extract	24	3
			625	µg/mL	Stenotrophomo nas maltophilia	Xanthom onadales	Gamma proteob acteria	Pseudom onadota	hydralcoholic -extract	hydralcohol ic-extract	hydralcohol ic-extract	24	3
			156	µg/mL	Candida albicans	Saccharo mycetale s	Sacchar omycet es	Ascomyc ota	hydralcoholic -extract	hydralcohol ic-extract	hydralcohol ic-extract	24	3
			39	µg/mL	Candida albicans	Saccharo mycetale s	Sacchar omycet es	Ascomyc ota	hydralcoholic -extract	hydralcohol ic-extract	hydralcohol ic-extract	24	3
			625	µg/mL	Candida albicans	Saccharo mycetale s	Sacchar omycet es	Ascomyc ota	hydralcoholic -extract	hydralcohol ic-extract	hydralcohol ic-extract	24	3
			2.23	µg/mL	Staphylococcus aureus	Bacillales	Bacilli	Bacillota	xanthohumul	chalcones	flavonoids	24	3
			2.32	µg/mL	Staphylococcus aureus	Bacillales	Bacilli	Bacillota	desmethylxa nthohumul	chalcones	flavonoids	24	3
			0.53	µg/mL	Staphylococcus aureus	Bacillales	Bacilli	Bacillota	lupulone	β-acids	bitter acids	24	3
			9.8	µg/mL	Staphylococcus aureus	Bacillales	Bacilli	Bacillota	xanthohumul	chalcones	flavonoids	24	3
			9.8	µg/mL	Staphylococcus aureus	Bacillales	Bacilli	Bacillota	xanthohumul	chalcones	flavonoids	24	3
			9.8	µg/mL	Staphylococcus aureus	Bacillales	Bacilli	Bacillota	xanthohumul	chalcones	flavonoids	24	3
			19.5	µg/mL	Staphylococcus aureus	Bacillales	Bacilli	Bacillota	xanthohumul	chalcones	flavonoids	24	3
			39	µg/mL	Staphylococcus aureus	Bacillales	Bacilli	Bacillota	desmethylxa nthohumul	chalcones	flavonoids	24	3
			19.5	µg/mL	Staphylococcus aureus	Bacillales	Bacilli	Bacillota	desmethylxa nthohumul	chalcones	flavonoids	24	3
			39	µg/mL	Staphylococcus aureus	Bacillales	Bacilli	Bacillota	desmethylxa nthohumul	chalcones	flavonoids	24	3
			39	µg/mL	Staphylococcus aureus	Bacillales	Bacilli	Bacillota	desmethylxa nthohumul	chalcones	flavonoids	24	3
			156	µg/mL	Staphylococcus aureus	Bacillales	Bacilli	Bacillota	cohumulone	α-acids	bitter acids	24	3
			313	µg/mL	Staphylococcus aureus	Bacillales	Bacilli	Bacillota	cohumulone	α-acids	bitter acids	24	3
			313	µg/mL	Staphylococcus aureus	Bacillales	Bacilli	Bacillota	cohumulone	α-acids	bitter acids	24	3
			313	µg/mL	Staphylococcus aureus	Bacillales	Bacilli	Bacillota	cohumulone	α-acids	bitter acids	24	3
			78	µg/mL	Staphylococcus aureus	Bacillales	Bacilli	Bacillota	humulone	α-acids	bitter acids	24	3
			156	µg/mL	Staphylococcus aureus	Bacillales	Bacilli	Bacillota	humulone	α-acids	bitter acids	24	3
			156	µg/mL	Staphylococcus aureus	Bacillales	Bacilli	Bacillota	humulone	α-acids	bitter acids	24	3
			156	µg/mL	Staphylococcus aureus	Bacillales	Bacilli	Bacillota	humulone	α-acids	bitter acids	24	3
			39	µg/mL	Staphylococcus aureus	Bacillales	Bacilli	Bacillota	colupulone	β-acids	bitter acids	24	3
			78	µg/mL	Staphylococcus aureus	Bacillales	Bacilli	Bacillota	colupulone	β-acids	bitter acids	24	3
			39	µg/mL	Staphylococcus aureus	Bacillales	Bacilli	Bacillota	colupulone	β-acids	bitter acids	24	3

			78	µg/mL	Staphylococcus aureus	Bacillales	Bacilli	Bacillota	colupulone	β-acids	bitter acids	24	3
			1.2	µg/mL	Staphylococcus aureus	Bacillales	Bacilli	Bacillota	lupulone	β-acids	bitter acids	24	3
			0.6	µg/mL	Staphylococcus aureus	Bacillales	Bacilli	Bacillota	lupulone	β-acids	bitter acids	24	3
			0.6	µg/mL	Staphylococcus aureus	Bacillales	Bacilli	Bacillota	lupulone	β-acids	bitter acids	24	3
			1.2	µg/mL	Staphylococcus aureus	Bacillales	Bacilli	Bacillota	lupulone	β-acids	bitter acids	24	3
181623 87	2008	P. Nataraj ana	3	µg/mL	Bacillus subtilis	Bacillales	Bacilli	Bacillota	humulone	α-acids	bitter acids	24	2
			5	µg/mL	Bacillus megaterium	Bacillales	Bacilli	Bacillota	humulone	α-acids	bitter acids	24	2
			30	µg/mL	Streptococcus salivarius	Lactobacillales	Bacilli	Bacillota	humulone	α-acids	bitter acids	24	2
			10	µg/mL	Streptococcus saprophyticus	Lactobacillales	Bacilli	Bacillota	humulone	α-acids	bitter acids	24	2
			1	µg/mL	Bacillus subtilis	Bacillales	Bacilli	Bacillota	lupulone	β-acids	bitter acids	24	2
			3	µg/mL	Bacillus megaterium	Bacillales	Bacilli	Bacillota	lupulone	β-acids	bitter acids	24	2
			5	µg/mL	Streptococcus salivarius	Lactobacillales	Bacilli	Bacillota	lupulone	β-acids	bitter acids	24	2
			1	µg/mL	Streptococcus saprophyticus	Lactobacillales	Bacilli	Bacillota	lupulone	β-acids	bitter acids	24	2
			1	µg/mL	Bacillus subtilis	Bacillales	Bacilli	Bacillota	xanthohumol	chalcones	flavonoids	24	2
			10	µg/mL	Bacillus megaterium	Bacillales	Bacilli	Bacillota	xanthohumol	chalcones	flavonoids	24	2
			10	µg/mL	Streptococcus salivarius	Lactobacillales	Bacilli	Bacillota	xanthohumol	chalcones	flavonoids	24	2
			1	µg/mL	Streptococcus saprophyticus	Lactobacillales	Bacilli	Bacillota	xanthohumol	chalcones	flavonoids	24	2
			3	µg/mL	Streptococcus saprophyticus	Lactobacillales	Bacilli	Bacillota	humulone	α-acids	bitter acids	24	2
			3	µg/mL	Bacillus subtilis	Bacillales	Bacilli	Bacillota	humulone	α-acids	bitter acids	24	2
			3	µg/mL	Streptococcus saprophyticus	Lactobacillales	Bacilli	Bacillota	lupulone	β-acids	bitter acids	24	2
			3	µg/mL	Bacillus subtilis	Bacillales	Bacilli	Bacillota	lupulone	β-acids	bitter acids	24	2
			10	µg/mL	Bacillus megaterium	Bacillales	Bacilli	Bacillota	lupulone	β-acids	bitter acids	24	2
			100	µg/mL	Streptococcus salivarius	Lactobacillales	Bacilli	Bacillota	lupulone	β-acids	bitter acids	24	2
			3	µg/mL	Streptococcus saprophyticus	Lactobacillales	Bacilli	Bacillota	xanthohumol	chalcones	flavonoids	24	2
			10	µg/mL	Bacillus subtilis	Bacillales	Bacilli	Bacillota	xanthohumol	chalcones	flavonoids	24	2
			10	µg/mL	Bacillus megaterium	Bacillales	Bacilli	Bacillota	xanthohumol	chalcones	flavonoids	24	2
			30	µg/mL	Streptococcus salivarius	Lactobacillales	Bacilli	Bacillota	xanthohumol	chalcones	flavonoids	24	2
			3	µg/mL	Streptococcus saprophyticus	Lactobacillales	Bacilli	Bacillota	humulone	α-acids	bitter acids	24	2
			3	µg/mL	Bacillus subtilis	Bacillales	Bacilli	Bacillota	humulone	α-acids	bitter acids	24	2
			3	µg/mL	Streptococcus saprophyticus	Lactobacillales	Bacilli	Bacillota	lupulone	β-acids	bitter acids	24	2
			3	µg/mL	Bacillus subtilis	Bacillales	Bacilli	Bacillota	lupulone	β-acids	bitter acids	24	2

			10	µg/mL	Bacillus megaterium	Bacillales	Bacilli	Bacillota	lupulone	β-acids	bitter acids	24	2
			100	µg/mL	Streptococcus salivarius	Lactobacillales	Bacilli	Bacillota	lupulone	β-acids	bitter acids	24	2
			3	µg/mL	Streptococcus saprophyticus	Lactobacillales	Bacilli	Bacillota	xanthohumol	chalcones	flavonoids	24	2
			10	µg/mL	Bacillus subtilis	Bacillales	Bacilli	Bacillota	xanthohumol	chalcones	flavonoids	24	2
			10	µg/mL	Bacillus megaterium	Bacillales	Bacilli	Bacillota	xanthohumol	chalcones	flavonoids	24	2
			30	µg/mL	Streptococcus salivarius	Lactobacillales	Bacilli	Bacillota	xanthohumol	chalcones	flavonoids	24	2
21317249	2011	Christina Engels	600	µg/mL	Bacillus subtilis	Bacillales	Bacilli	Bacillota	catechin	flavonols	flavonoids	48	3
			1300	µg/mL	Bacillus subtilis	Bacillales	Bacilli	Bacillota	catechin	flavonols	flavonoids	48	3
			1700	µg/mL	Bacillus subtilis	Bacillales	Bacilli	Bacillota	catechin	flavonols	flavonoids	48	3
			100	µg/mL	Bacillus cereus	Bacillales	Bacilli	Bacillota	catechin	flavonols	flavonoids	48	3
			100	µg/mL	Staphylococcus aureus	Bacillales	Bacilli	Bacillota	catechin	flavonols	flavonoids	48	3
			500	µg/mL	Listeria monocytogenes	Bacillales	Bacilli	Bacillota	catechin	flavonols	flavonoids	48	3
			1700	µg/mL	Pediococcus acidilactici	Lactobacillales	Bacilli	Bacillota	catechin	flavonols	flavonoids	48	3
			1700	µg/mL	Lactococcus lactis	Lactobacillales	Bacilli	Bacillota	catechin	flavonols	flavonoids	48	3
			1700	µg/mL	Pseudomonas fluorescens	Pseudomonadales	Gamma proteobacteria	Pseudomonadota	catechin	flavonols	flavonoids	48	3
			300	µg/mL	Bacillus amyloliquefaciens	Bacillales	Bacilli	Bacillota	catechin	flavonols	flavonoids	48	3
			100	µg/mL	Staphylococcus warneri	Bacillales	Bacilli	Bacillota	catechin	flavonols	flavonoids	48	3
			1700	µg/mL	Lactobacillus plantarum	Lactobacillales	Bacilli	Bacillota	catechin	flavonols	flavonoids	48	3
			1700	µg/mL	Enterococcus faecalis	Lactobacillales	Bacilli	Bacillota	catechin	flavonols	flavonoids	48	3
			1700	µg/mL	Pseudomonas fluorescens	Pseudomonadales	Gamma proteobacteria	Pseudomonadota	catechin	flavonols	flavonoids	48	3
			1700	µg/mL	Pseudomonas fluorescens	Pseudomonadales	Gamma proteobacteria	Pseudomonadota	catechin	flavonols	flavonoids	48	3
			600	µg/mL	Campylobacter jejuni	Campylobacteres	Campylobacteriia	Campylobacterota	catechin	flavonols	flavonoids	48	3
			1700	µg/mL	Mucor plumbeus	Mucorales	Phycomycetes	Mucoromycota	catechin	flavonols	flavonoids	48	3
			1700	µg/mL	Aspergillus niger	Eurotiales	Eurotiomycetes	Ascomycota	catechin	flavonols	flavonoids	48	3
			26.8	µg/mL	Penicillium spp	Eurotiales	Eurotiomycetes	Ascomycota	catechin	flavonols	flavonoids	48	3
			31	µg/mL	Streptococcus aureus	Lactobacillales	Bacilli	Bacillota	hydraulic-hollic-extract	hydraulic-hollic-extract	hydraulic-hollic-extract	24	4
			125	µg/mL	Streptococcus aureus	Lactobacillales	Bacilli	Bacillota	hydraulic-hollic-extract	hydraulic-hollic-extract	hydraulic-hollic-extract	24	4
			31	µg/mL	Streptococcus aureus	Lactobacillales	Bacilli	Bacillota	hydraulic-hollic-extract	hydraulic-hollic-extract	hydraulic-hollic-extract	24	4
			62	µg/mL	Enterococcus faecalis	Lactobacillales	Bacilli	Bacillota	hydraulic-hollic-extract	hydraulic-hollic-extract	hydraulic-hollic-extract	24	4
			15	µg/mL	Streptococcus aureus	Lactobacillales	Bacilli	Bacillota	xanthohumol	chalcones	flavonoids	24	4

24175280	2013	Marcin Rozalski	125	µg/mL	Streptococcus aureus	Lactobacillales	Bacilli	Bacillota	xanthohumol	chalcones	flavonoids	24	4
			93.5	µg/mL	Streptococcus aureus	Lactobacillales	Bacilli	Bacillota	xanthohumol	chalcones	flavonoids	24	4
			62	µg/mL	Enterococcus faecalis	Lactobacillales	Bacilli	Bacillota	xanthohumol	chalcones	flavonoids	24	4
			2000	µg/mL	Streptococcus aureus	Lactobacillales	Bacilli	Bacillota	CO2-extract	CO2-extract	CO2-extract	24	4
			1000	µg/mL	Streptococcus aureus	Lactobacillales	Bacilli	Bacillota	CO2-extract	CO2-extract	CO2-extract	24	4
			2000	µg/mL	Streptococcus aureus	Lactobacillales	Bacilli	Bacillota	CO2-extract	CO2-extract	CO2-extract	24	4
			2000	µg/mL	Enterococcus faecalis	Lactobacillales	Bacilli	Bacillota	CO2-extract	CO2-extract	CO2-extract	24	4
			31	µg/mL	Streptococcus aureus	Lactobacillales	Bacilli	Bacillota	xanthohumol	chalcones	flavonoids	24	4
			125	µg/mL	Streptococcus aureus	Lactobacillales	Bacilli	Bacillota	xanthohumol	chalcones	flavonoids	24	4
			31	µg/mL	Streptococcus aureus	Lactobacillales	Bacilli	Bacillota	xanthohumol	chalcones	flavonoids	24	4
			62	µg/mL	Enterococcus faecalis	Lactobacillales	Bacilli	Bacillota	xanthohumol	chalcones	flavonoids	24	4
20409652	2010	Jaroslav Flesar	2	µg/mL	Paenibacillus larvae	Bacillales	Bacilli	Bacillota	organic-ethanolic extract	organic-ethanolic extract	organic-ethanolic extract	48	3
			3	µg/mL	Paenibacillus larvae	Bacillales	Bacilli	Bacillota	organic extract	organic extract	organic extract	48	3
			128	µg/mL	Paenibacillus larvae	Bacillales	Bacilli	Bacillota	catechin	flavonols	flavonoids	48	3
			30	µg/mL	Staphylococcus aureus	Bacillales	Bacilli	Bacillota	humulone	α-acids	bitter acids	24	4
			60	µg/mL	Enterococcus faecalis	Lactobacillales	Bacilli	Bacillota	humulone	α-acids	bitter acids	24	4
			60	µg/mL	Staphylococcus aureus	Bacillales	Bacilli	Bacillota	humulone	α-acids	bitter acids	24	4
			60	µg/mL	Enterococcus faecalis	Lactobacillales	Bacilli	Bacillota	humulone	α-acids	bitter acids	24	4
			30	µg/mL	Staphylococcus haemolyticus	Bacillales	Bacilli	Bacillota	humulone	α-acids	bitter acids	24	4
			250	µg/mL	Candida albicans	Saccharomycetales	Saccharomycetes	Ascomycota	humulone	α-acids	bitter acids	48	4
			250	µg/mL	Candida krusei	Saccharomycetales	Saccharomycetes	Ascomycota	humulone	α-acids	bitter acids	48	4
			1.000	µg/mL	Candida tropicalis	Saccharomycetales	Saccharomycetes	Ascomycota	humulone	α-acids	bitter acids	48	4
			500	µg/mL	Candida parapsilosis	Saccharomycetales	Saccharomycetes	Ascomycota	humulone	α-acids	bitter acids	48	4
			0.5	µg/mL	Staphylococcus aureus	Bacillales	Bacilli	Bacillota	lupulone	β-acids	bitter acids	24	4
			1.5	µg/mL	Enterococcus faecalis	Lactobacillales	Bacilli	Bacillota	lupulone	β-acids	bitter acids	24	4
			1	µg/mL	Staphylococcus aureus	Bacillales	Bacilli	Bacillota	lupulone	β-acids	bitter acids	24	4
			15	µg/mL	Enterococcus faecalis	Lactobacillales	Bacilli	Bacillota	lupulone	β-acids	bitter acids	24	4
			1	µg/mL	Staphylococcus haemolyticus	Bacillales	Bacilli	Bacillota	lupulone	β-acids	bitter acids	24	4
			500	µg/mL	Candida albicans	Saccharomycetales	Saccharomycetes	Ascomycota	lupulone	β-acids	bitter acids	48	4

29790489	2018	Katerina Bogdanova	500	µg/mL	Candida krusei	Saccharomycetales	Saccharomycetes	Ascomycota	lupulone	β-acids	bitter acids	48	4
			1.000	µg/mL	Candida parapsilosis	Saccharomycetales	Saccharomycetes	Ascomycota	lupulone	β-acids	bitter acids	48	4
			4	µg/mL	Staphylococcus aureus	Bacillales	Bacilli	Bacillota	xanthohumol	chalcones	flavonoids	24	4
			7.5	µg/mL	Enterococcus faecalis	Lactobacillales	Bacilli	Bacillota	xanthohumol	chalcones	flavonoids	24	4
			4	µg/mL	Staphylococcus aureus	Bacillales	Bacilli	Bacillota	xanthohumol	chalcones	flavonoids	24	4
			7.5	µg/mL	Enterococcus faecalis	Lactobacillales	Bacilli	Bacillota	xanthohumol	chalcones	flavonoids	24	4
			7.5	µg/mL	Staphylococcus haemolyticus	Bacillales	Bacilli	Bacillota	xanthohumol	chalcones	flavonoids	24	4
			60	µg/mL	Candida albicans	Saccharomycetales	Saccharomycetes	Ascomycota	xanthohumol	chalcones	flavonoids	48	4
			60	µg/mL	Candida krusei	Saccharomycetales	Saccharomycetes	Ascomycota	xanthohumol	chalcones	flavonoids	48	4
			30	µg/mL	Candida tropicalis	Saccharomycetales	Saccharomycetes	Ascomycota	xanthohumol	chalcones	flavonoids	48	4
			7.5	µg/mL	Candida parapsilosis	Saccharomycetales	Saccharomycetes	Ascomycota	xanthohumol	chalcones	flavonoids	48	4
			7.5	µg/mL	Staphylococcus aureus	Bacillales	Bacilli	Bacillota	CO2-extract	CO2-extract	CO2-extract	24	4
			60	µg/mL	Enterococcus faecalis	Lactobacillales	Bacilli	Bacillota	CO2-extract	CO2-extract	CO2-extract	24	4
			7.5	µg/mL	Staphylococcus aureus	Bacillales	Bacilli	Bacillota	CO2-extract	CO2-extract	CO2-extract	24	4
			30	µg/mL	Enterococcus faecalis	Lactobacillales	Bacilli	Bacillota	CO2-extract	CO2-extract	CO2-extract	24	4
			15	µg/mL	Staphylococcus haemolyticus	Bacillales	Bacilli	Bacillota	CO2-extract	CO2-extract	CO2-extract	24	4
			250	µg/mL	Candida albicans	Saccharomycetales	Saccharomycetes	Ascomycota	CO2-extract	CO2-extract	CO2-extract	48	4
			250	µg/mL	Candida krusei	Saccharomycetales	Saccharomycetes	Ascomycota	CO2-extract	CO2-extract	CO2-extract	48	4
			1.000	µg/mL	Candida tropicalis	Saccharomycetales	Saccharomycetes	Ascomycota	CO2-extract	CO2-extract	CO2-extract	48	4
			500	µg/mL	Candida parapsilosis	Saccharomycetales	Saccharomycetes	Ascomycota	CO2-extract	CO2-extract	CO2-extract	48	4
32123428	2020	M.L. Bhavya	64	µg/mL	Staphylococcus aureus	Bacillales	Bacilli	Bacillota	CO2-extract	CO2-extract	CO2-extract	48	4
			32	µg/mL	Listeria monocytogenes	Bacillales	Bacilli	Bacillota	CO2-extract	CO2-extract	CO2-extract	48	4
			32	µg/mL	Bacillus subtilis	Bacillales	Bacilli	Bacillota	CO2-extract	CO2-extract	CO2-extract	48	4
			256	µg/mL	Bifidobacterium dentium	Bifidobacteriales	Actinomycetia	Actinomycetota	hydraulic-hollic-extract	hydraulic-hollic-extract	hydraulic-hollic-extract	48	3
			128	µg/mL	Bifidobacterium dentium	Bifidobacteriales	Actinomycetia	Actinomycetota	hydraulic-hollic-extract	hydraulic-hollic-extract	hydraulic-hollic-extract	48	3
			256	µg/mL	Bifidobacterium dentium	Bifidobacteriales	Actinomycetia	Actinomycetota	hydraulic-hollic-extract	hydraulic-hollic-extract	hydraulic-hollic-extract	48	3
			256	µg/mL	Bifidobacterium dentium	Bifidobacteriales	Actinomycetia	Actinomycetota	hydraulic-hollic-extract	hydraulic-hollic-extract	hydraulic-hollic-extract	48	3

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			64	µg/mL	Streptococcus sobrinus	Lactobacillales	Bacilli	Bacillota	hydralcoholic-extract	hydralcoholic-extract	hydralcoholic-extract	48	3
			16	µg/mL	Streptococcus sobrinus	Lactobacillales	Bacilli	Bacillota	hydralcoholic-extract	hydralcoholic-extract	hydralcoholic-extract	48	3
			64	µg/mL	Streptococcus sobrinus	Lactobacillales	Bacilli	Bacillota	hydralcoholic-extract	hydralcoholic-extract	hydralcoholic-extract	48	3
			64	µg/mL	Streptococcus sobrinus	Lactobacillales	Bacilli	Bacillota	hydralcoholic-extract	hydralcoholic-extract	hydralcoholic-extract	48	3
			128	µg/mL	Streptococcus sobrinus	Lactobacillales	Bacilli	Bacillota	hydralcoholic-extract	hydralcoholic-extract	hydralcoholic-extract	48	3
			64	µg/mL	Streptococcus sobrinus	Lactobacillales	Bacilli	Bacillota	hydralcoholic-extract	hydralcoholic-extract	hydralcoholic-extract	48	3
			512	µg/mL	Eikenella corrodens	Neisseriales	Betaproteobacteria	Pseudomonadota	hydralcoholic-extract	hydralcoholic-extract	hydralcoholic-extract	48	3
			256	µg/mL	Fusobacterium nucleatum	Fusobacteriales	Fusobacteriia	Fusobacteriota	hydralcoholic-extract	hydralcoholic-extract	hydralcoholic-extract	48	3
			256	µg/mL	Fusobacterium nucleatum	Fusobacteriales	Fusobacteriia	Fusobacteriota	hydralcoholic-extract	hydralcoholic-extract	hydralcoholic-extract	48	3
			512	µg/mL	Fusobacterium nucleatum	Fusobacteriales	Fusobacteriia	Fusobacteriota	hydralcoholic-extract	hydralcoholic-extract	hydralcoholic-extract	48	3
			256	µg/mL	Fusobacterium nucleatum	Fusobacteriales	Fusobacteriia	Fusobacteriota	hydralcoholic-extract	hydralcoholic-extract	hydralcoholic-extract	48	3
			512	µg/mL	Fusobacterium nucleatum	Fusobacteriales	Fusobacteriia	Fusobacteriota	hydralcoholic-extract	hydralcoholic-extract	hydralcoholic-extract	48	3
			512	µg/mL	Fusobacterium nucleatum	Fusobacteriales	Fusobacteriia	Fusobacteriota	hydralcoholic-extract	hydralcoholic-extract	hydralcoholic-extract	48	3
			128	µg/mL	Fusobacterium nucleatum	Fusobacteriales	Fusobacteriia	Fusobacteriota	hydralcoholic-extract	hydralcoholic-extract	hydralcoholic-extract	48	3
			64	µg/mL	Fusobacterium nucleatum	Fusobacteriales	Fusobacteriia	Fusobacteriota	hydralcoholic-extract	hydralcoholic-extract	hydralcoholic-extract	48	3
			128	µg/mL	Fusobacterium nucleatum	Fusobacteriales	Fusobacteriia	Fusobacteriota	hydralcoholic-extract	hydralcoholic-extract	hydralcoholic-extract	48	3
			128	µg/mL	Fusobacterium nucleatum	Fusobacteriales	Fusobacteriia	Fusobacteriota	hydralcoholic-extract	hydralcoholic-extract	hydralcoholic-extract	48	3
			128	µg/mL	Fusobacterium nucleatum	Fusobacteriales	Fusobacteriia	Fusobacteriota	hydralcoholic-extract	hydralcoholic-extract	hydralcoholic-extract	48	3
			128	µg/mL	Fusobacterium nucleatum	Fusobacteriales	Fusobacteriia	Fusobacteriota	hydralcoholic-extract	hydralcoholic-extract	hydralcoholic-extract	48	3
			256	µg/mL	Candida albicans	Saccharomycetales	Saccharomycetes	Ascomycota	hydralcoholic-extract	hydralcoholic-extract	hydralcoholic-extract	48	3
			256	µg/mL	Candida albicans	Saccharomycetales	Saccharomycetes	Ascomycota	hydralcoholic-extract	hydralcoholic-extract	hydralcoholic-extract	48	3
			512	µg/mL	Candida albicans	Saccharomycetales	Saccharomycetes	Ascomycota	hydralcoholic-extract	hydralcoholic-extract	hydralcoholic-extract	48	3
			512	µg/mL	Candida albicans	Saccharomycetales	Saccharomycetes	Ascomycota	hydralcoholic-extract	hydralcoholic-extract	hydralcoholic-extract	48	3
			1.8	µg/mL	Bacillus subtilis	Bacillales	Bacilli	Bacillota	4-Deoxytetrahydro-cohumulone	α-acids	bitter acids	24	3
			9	µg/mL	Bacillus subtilis	Bacillales	Bacilli	Bacillota	4-Deoxy-cohumulone	α-acids	bitter acids	24	3

803401	1974	Arno Schmalr eck	11	µg/mL	Bacillus subtilis	Bacillales	Bacilli	Bacillota	humulone	α-acids	bitter acids	24	3
			22	µg/mL	Bacillus subtilis	Bacillales	Bacilli	Bacillota	5-prenyl- isocohumulo ne	α-acids	bitter acids	24	3
			30	µg/mL	Bacillus subtilis	Bacillales	Bacilli	Bacillota	6-hydroxy- colupulone	α-acids	bitter acids	24	3
			75	µg/mL	Bacillus subtilis	Bacillales	Bacilli	Bacillota	isohumulone	α-acids	bitter acids	24	3
			920	µg/mL	Bacillus subtilis	Bacillales	Bacilli	Bacillota	2-peroxy- colupulone	α-acids	bitter acids	24	3
315953 44	2019	Natalia Janaina Lago Maia	1.00 0	µg/mL	Saccharomyces cerevisiae	Saccharo mycetale s	Sacchar omycet es	Ascomyc ota	CO2-extract	CO2-extract	CO2-extract	24	6
			5	µg/mL	Lactobacillus fermentum	Lactobac illales	Bacilli	Bacillota	CO2-extract	CO2-extract	CO2-extract	24	6
			5	µg/mL	Leuconostoc mesenteroides	Lactobac illales	Bacilli	Bacillota	CO2-extract	CO2-extract	CO2-extract	24	6
249489 53	2014	Jian Wei	10	µg/mL	Mycobacterium tuberculosis	Mycobac teriales	Actinom ycetia	Actinomy cetota	lupulone	β-acids	bitter acids	48	2
366162 49	2022	Zala Kolenc	15.6	µg/mL	Staphylococcus aureus	Bacillales	Bacilli	Bacillota	hydroacetoni c-extract	hydroaceto nic-extract	hydroaceto nic-extract	24	4
			19.5	µg/mL	Staphylococcus aureus	Bacillales	Bacilli	Bacillota	hydroacetoni c-extract	hydroaceto nic-extract	hydroaceto nic-extract	24	4
			15.6	µg/mL	Staphylococcus aureus	Bacillales	Bacilli	Bacillota	hydroacetoni c-extract	hydroaceto nic-extract	hydroaceto nic-extract	24	4
			9.8	µg/mL	Staphylococcus aureus	Bacillales	Bacilli	Bacillota	hydroacetoni c-extract	hydroaceto nic-extract	hydroaceto nic-extract	24	4
			19.5	µg/mL	Staphylococcus aureus	Bacillales	Bacilli	Bacillota	hydroacetoni c-extract	hydroaceto nic-extract	hydroaceto nic-extract	24	4
			19.5	µg/mL	Staphylococcus aureus	Bacillales	Bacilli	Bacillota	hydroacetoni c-extract	hydroaceto nic-extract	hydroaceto nic-extract	24	4
			19.5	µg/mL	Staphylococcus aureus	Bacillales	Bacilli	Bacillota	hydroacetoni c-extract	hydroaceto nic-extract	hydroaceto nic-extract	24	4
			27.3	µg/mL	Staphylococcus aureus	Bacillales	Bacilli	Bacillota	hydroacetoni c-extract	hydroaceto nic-extract	hydroaceto nic-extract	24	4
			31.3	µg/mL	Staphylococcus aureus	Bacillales	Bacilli	Bacillota	hydroacetoni c-extract	hydroaceto nic-extract	hydroaceto nic-extract	24	4
			31.3	µg/mL	Staphylococcus aureus	Bacillales	Bacilli	Bacillota	hydroacetoni c-extract	hydroaceto nic-extract	hydroaceto nic-extract	24	4
			15.6	µg/mL	Staphylococcus aureus	Bacillales	Bacilli	Bacillota	hydroacetoni c-extract	hydroaceto nic-extract	hydroaceto nic-extract	24	4
			54.7	µg/mL	Staphylococcus aureus	Bacillales	Bacilli	Bacillota	hydroacetoni c-extract	hydroaceto nic-extract	hydroaceto nic-extract	24	4
			250	µg/mL	Staphylococcus aureus	Bacillales	Bacilli	Bacillota	hydroacetoni c-extract	hydroaceto nic-extract	hydroaceto nic-extract	24	4
			250	µg/mL	Staphylococcus aureus	Bacillales	Bacilli	Bacillota	hydroacetoni c-extract	hydroaceto nic-extract	hydroaceto nic-extract	24	4
			62.5	µg/mL	Lactobacillus acidophilus	Lactobac illales	Bacilli	Bacillota	hydroacetoni c-extract	hydroaceto nic-extract	hydroaceto nic-extract	48	4
			62.5	µg/mL	Lactobacillus acidophilus	Lactobac illales	Bacilli	Bacillota	hydroacetoni c-extract	hydroaceto nic-extract	hydroaceto nic-extract	48	4
			83.3	µg/mL	Lactobacillus acidophilus	Lactobac illales	Bacilli	Bacillota	hydroacetoni c-extract	hydroaceto nic-extract	hydroaceto nic-extract	48	4

			62.5	µg/mL	Lactobacillus acidophilus	Lactobacillales	Bacilli	Bacillota	hydroacetonic-extract	hydroacetonic-extract	hydroacetonic-extract	48	4
			104.2	µg/mL	Lactobacillus acidophilus	Lactobacillales	Bacilli	Bacillota	hydroacetonic-extract	hydroacetonic-extract	hydroacetonic-extract	48	4
			83.3	µg/mL	Lactobacillus acidophilus	Lactobacillales	Bacilli	Bacillota	hydroacetonic-extract	hydroacetonic-extract	hydroacetonic-extract	48	4
			104.2	µg/mL	Lactobacillus acidophilus	Lactobacillales	Bacilli	Bacillota	hydroacetonic-extract	hydroacetonic-extract	hydroacetonic-extract	48	4
			62.5	µg/mL	Lactobacillus acidophilus	Lactobacillales	Bacilli	Bacillota	hydroacetonic-extract	hydroacetonic-extract	hydroacetonic-extract	48	4
			125	µg/mL	Lactobacillus acidophilus	Lactobacillales	Bacilli	Bacillota	hydroacetonic-extract	hydroacetonic-extract	hydroacetonic-extract	48	4
			208.3	µg/mL	Lactobacillus acidophilus	Lactobacillales	Bacilli	Bacillota	hydroacetonic-extract	hydroacetonic-extract	hydroacetonic-extract	48	4
			104.2	µg/mL	Lactobacillus acidophilus	Lactobacillales	Bacilli	Bacillota	hydroacetonic-extract	hydroacetonic-extract	hydroacetonic-extract	48	4
			83.3	µg/mL	Lactobacillus acidophilus	Lactobacillales	Bacilli	Bacillota	hydroacetonic-extract	hydroacetonic-extract	hydroacetonic-extract	48	4
			62.5	µg/mL	Lactobacillus acidophilus	Lactobacillales	Bacilli	Bacillota	hydroacetonic-extract	hydroacetonic-extract	hydroacetonic-extract	48	4
			83.3	µg/mL	Lactobacillus acidophilus	Lactobacillales	Bacilli	Bacillota	hydroacetonic-extract	hydroacetonic-extract	hydroacetonic-extract	48	4

Table 4: Characteristics of studies being used for meta-analysis process. The table illustrates the PMID, year of publication and the author; MIC value, Strains and the stratification of them in Order, Class, Phylum, Classes of compounds (1,2,3), time of incubation and number of experiments.

3.3.1 Results of meta-analysis in classcompound1

At first, we observed the data from meta-analysis of random effect model of classcompound1, for different compounds and extracts in classcompound1 during 24 and 48 hours of incubation against different microorganisms.

3.3.1.1 By strain

The diagrams here illustrate the meta-analysis of classcompound1 against the stratification of microorganisms in strains.

Table 5: Results of meta-analysis process. The table illustrates MIC value along with Confidence Interval (CI), p-value after meta-analysis of classcompound1 against different strains for 24 hours incubation. Finally, it shows the number of studies being used.

Hours	Number of studies	Strain	Classcompound1	MIC	CI (low - upper boundary)	p-value
24	3	Staphylococcus epidermidis	xanthohumol	1,37	0,123-2,609	0,027
24	10	Staphylococcus aureus	xanthohumol	6,53	3,048-10,014	0
24	3	Bacillus subtilis	xanthohumol	7,00	1,12-12,88	0
24	3	Bacillus megaterium	xanthohumol	10,00	9,2-10,8	1
24	3	Streptococcus salivarius	xanthohumol	23,33	10,267-36,4	0
24	3	Streptococcus saprophyticus	xanthohumol	2,33	1,027-3,64	0,069
24	6	Streptococcus aureus	xanthohumol	70,08	29,806-110,361	0
24	2	Enterococcus faecalis	xanthohumol	62,00	61,307-62,693	1
24	2	Staphylococcus epidermidis	humulone	18,75	(-)3,3-40,8	0
24	8	Staphylococcus aureus	humulone	83,25	39,867-126,633	0
24	4	Bacillus subtilis	humulone	5,01	0,33-9,692	0
24	3	Streptococcus saprophyticus	humulone	5,31	1,196-9,421	0

24	2	Enterococcus faecalis	humulone	60,00	59,307-60,693	0
24	2	Staphylococcus epidermidis	lupulone	2,25	(-)-1,18-5,68	0
24	8	Staphylococcus aureus	lupulone	0,76	0,377-1,146	0,947
24	3	Bacillus subtilis	lupulone	2,33	1,027-3,64	0
24	3	Bacillus megaterium	lupulone	7,67	3,093-12,24	0
24	3	Streptococcus salivarius	lupulone	68,33	6,268-130,399	0
24	3	Streptococcus saprophyticus	lupulone	2,33	1,027-3,64	0,069

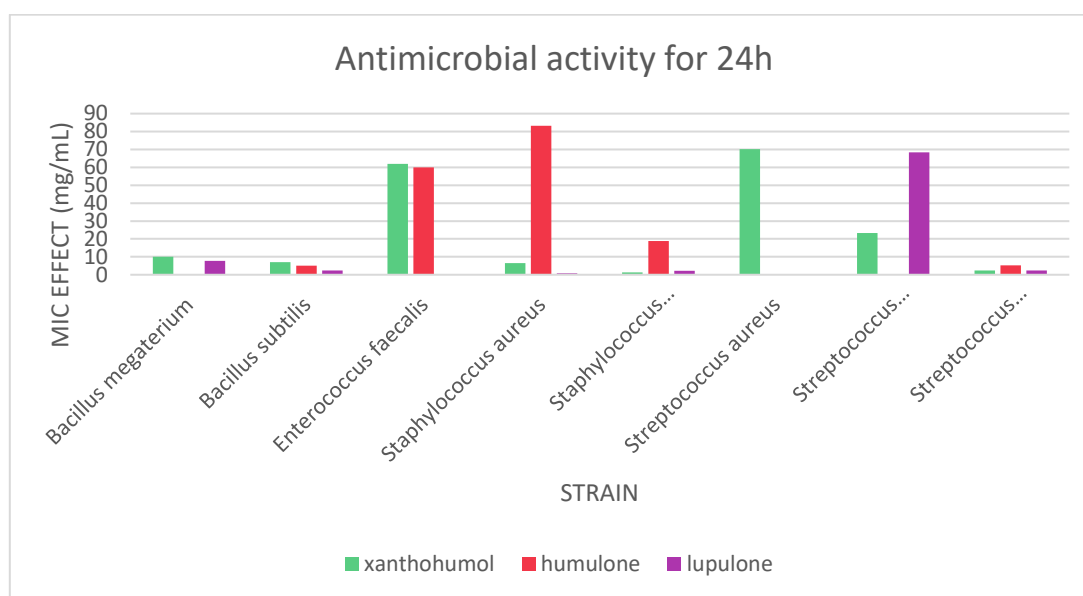


Figure 12: Minimum Inhibitory Concentration of meta-analysis for three hop compounds, against different microorganisms after 24h incubation. Green color stands for xanthohumol, red for humulone, purple for lupulone.

Table 6: Results of meta-analysis process. The table illustrates MIC value along with Confidence Interval (CI), p-value after meta-analysis of classcompound1 against different strains for 48-hours incubation. Finally it shows the number of studies being used.

Hours	Number of studies	Strain	Classcompound1	MIC	CI (low - upper boundary)	p-value
48	7	Bacteroides fragilis	xanthohumol	39,43	27,795-51,062	0
48	5	Clostridium perfringens	xanthohumol	32,60	18,719-46,481	0

48	28	Clostridium difficile	xanthohumol	59,04	51,644-66,428	0
48	2	Propionibacterium acnes	xanthohumol	46,88	16,251-77,499	0

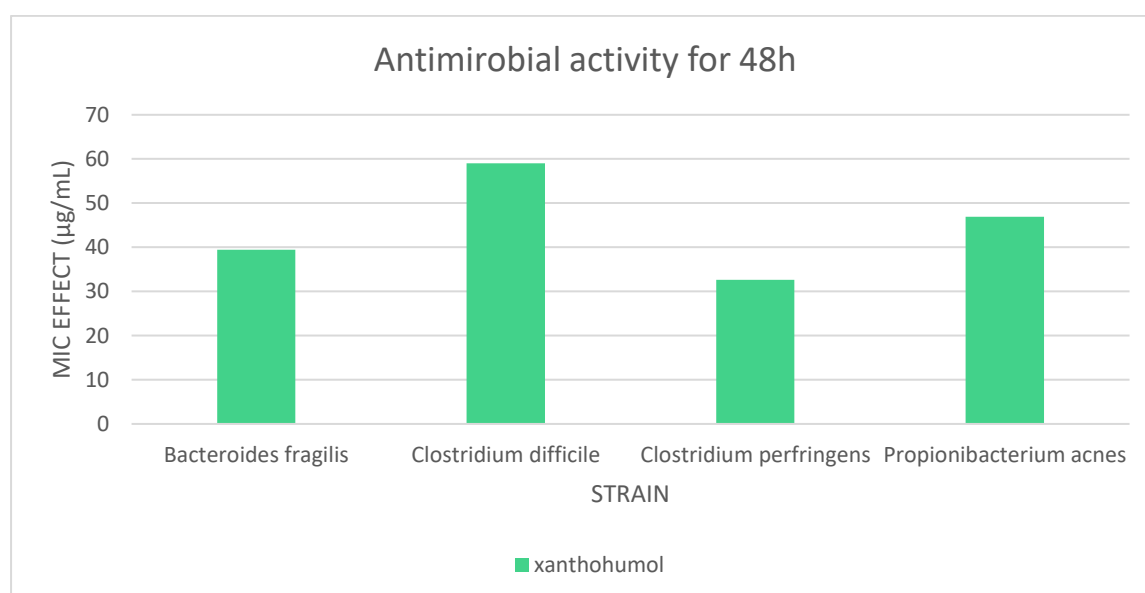


Figure 13: Minimum Inhibitory Concentration of meta-analysis for compound against microorganisms after 48h incubation. Green color stands for xanthohumol

Table 7: Results of meta-analysis process. The table illustrates MIC value along with Confidence Interval (CI), p-value after meta-analysis of classcompound1 extracts against different strains for 24-hours incubation. Finally it shows the number of studies being used.

Hours	Number of studies	Strain	Classcompound1	MIC	CI (low - upper boundary)	p-value
24	4	Propionibacterium acnes	CO2-extract	3,49	2,728-4,247	0,144
24	6	Staphylococcus aureus	CO2-extract	6,32	2,205-10,425	0
24	2	Listeria monocytogenes	CO2-extract	10,00	9,307-10,693	1
24	2	Staphylococcus epidermidis	CO2-extract	0,10	(-)0,702-0,898	1
24	3	Streptococcus aureus	CO2-extract	1666,67	1013,345-2319,988	0
24	2	Enterococcus faecalis	Hydralcoholic-extract	50,50	27,962-73,041	0

24	2	Staphylococcus aureus	Hydralcoholic-extract	39,00	38,2-39,8	1
24	2	Staphylococcus epidermidis	Hydralcoholic-extract	68,50	10,681-126,319	0
24	2	Staphylococcus lugdunensis	Hydralcoholic-extract	390,50	(-)69,112-850,112	0
24	2	Staphylococcus warneri	Hydralcoholic-extract	332,00	(-)242,269-906,269	0
24	2	Streptococcus agalactiae	Hydralcoholic-extract	58,50	20,281-96,719	0
24	2	Pseudomonas aeruginosa	Hydralcoholic-extract	625,00	624,2-625,8	1
24	3	Candida albicans	Hydralcoholic-extract	273,33	(-)77,594-624,261	0
24	3	Streptococcus aureus	Hydralcoholic-extract	62,33	0,921-123,746	0
24	14	Staphylococcus aureus	Hydroacetic-extract	55,66	12,151-99,163	0

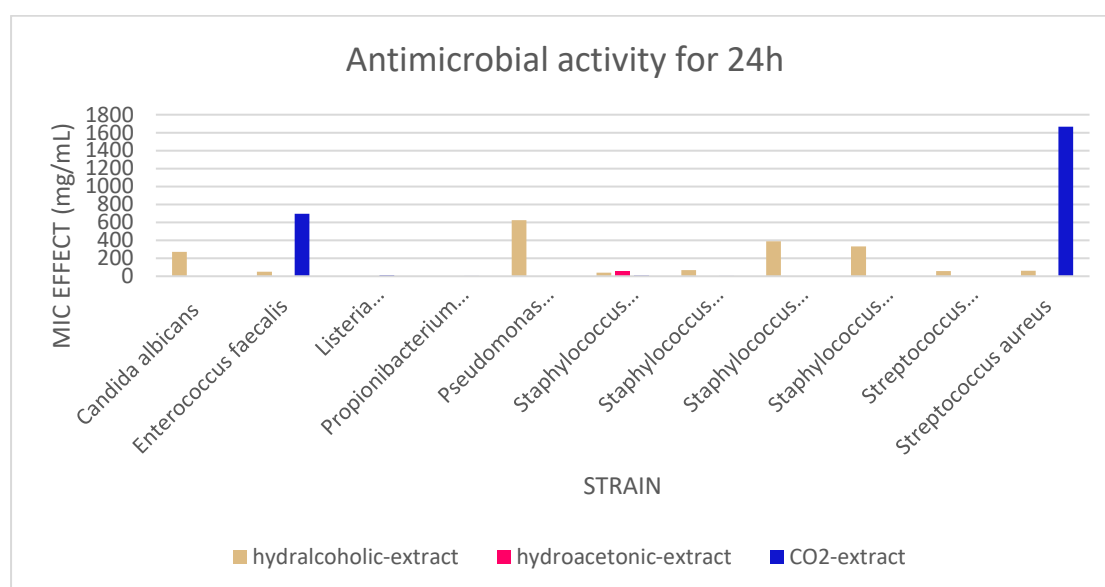


Figure 14: Minimum Inhibitory Concentration of hop extracts against microorganisms after 24h incubation. Beige color stands for hydralcoholic-extract, pink for hydroacetic-extract, blue for CO₂-extract

Table 8: Results of meta-analysis process. The table illustrates MIC value along with Confidence Interval (CI), p-value after meta-analysis of classcompound1 against different strains for 48-hours incubation. Finally, it shows the number of studies being used.

Hours	Number of studies	Strain	Classcompound1	MIC	CI (low - upper boundary)	p-value
48	7	Staphylococcus aureus	CO2-extract	46,43	(-)6,222-99,080	0
48	7	Listeria monocytogenes	CO2-extract	37,19	(-)16,563-90,934	0
48	6	Escherichia coli	CO2-extract	2604,17	1041,287-4167,047	0
48	6	Salmonella enterica	CO2-extract	2604,17	1041,287-4167,047	0
48	2	Streptococcus mutans	CO2-extract	0,39	(-)0,409-1,191	1
48	2	Streptococcus sanguinis	CO2-extract	0,78	(-)0,019-1,581	1
48	4	Propionibacterium acnes	CO2-extract	15,63	15,059-16,191	1
48	6	Bifidobacterium dentium	Hydralcoholic-extract	213,33	160,444-266,223	0
48	6	Bifidobacterium longum	Hydralcoholic-extract	96,00	67,951-124,049	0
48	6	Lactobacillus salivarius	Hydralcoholic-extract	138,67	88,318-189,016	0
48	6	Streptococcus mutans	Hydralcoholic-extract	106,67	80,222-133,111	0
48	6	Streptococcus salivarius	Hydralcoholic-extract	34,67	22,079-47,254	0
48	6	Streptococcus sobrinus	Hydralcoholic-extract	66,67	38,135-95,198	0
48	12	Fusobacterium nucleatum	Hydralcoholic-extract	250,67	154,914-346,419	0
48	4	Candida albicans	Hydralcoholic-extract	384,00	239,157-528,843	0

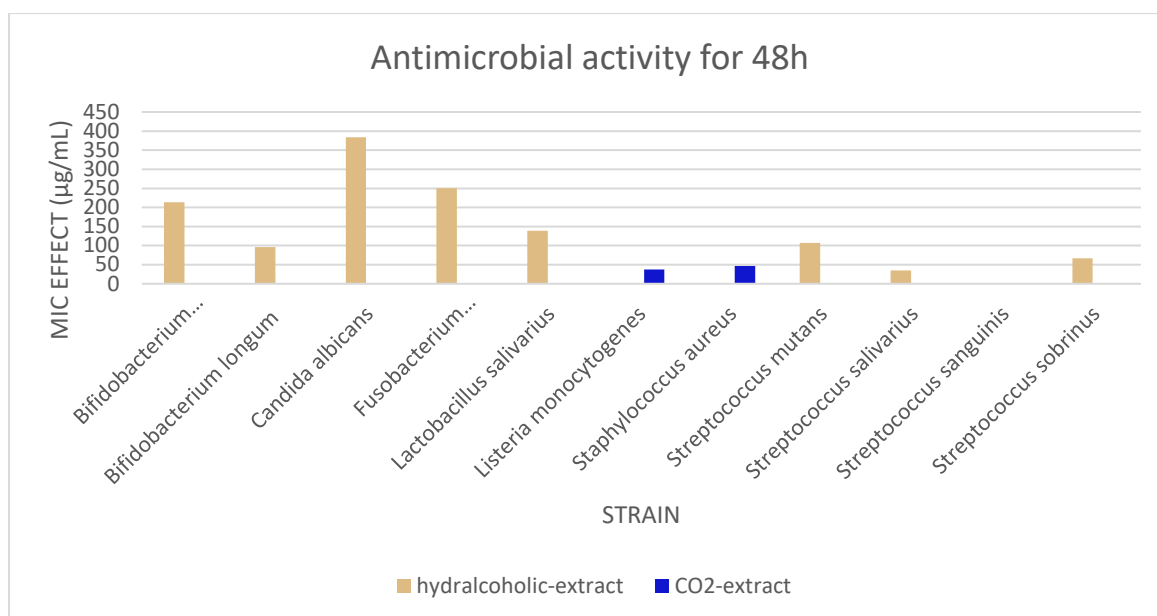


Figure 15: Minimum Inhibitory Concentration of meta-analysis for hop extracts against microorganisms after 48h incubation. Blue color stands for CO₂-extract and beige for hydalcoholic-extract.

To be more specific, we observed that xanthohumol in 24h incubation has, among most of the strains, strong antimicrobial activity, especially in *Staphylococcus aureus*, with MIC value equal to 6,53 µg/mL, being followed by *Streptococcus salivarius* (MIC:23,33 µg/mL) and *Staphylococcus epidermidis* (MIC:1,37 µg/mL).

It is significant to underline the strong antimicrobial activity during 24h incubation which has the CO₂-extract against *Staphylococcus epidermidis* (MIC: 0,10 µg/mL), while another important is during 48h incubation of CO₂-extract against *Streptococcus mutans* (MIC:0,39 µg/mL) than the hydalcoholic-extract with MIC equal to 68,5 µg/mL and 106,67 µg/mL correspondingly.

3.3.1.2 By phylum

The diagrams here illustrate the meta-analysis of classcompound1 against the stratification of microorganisms into the Phylum they belong.

Table 9: Results of meta-analysis process. The table illustrates MIC value along with Confidence Interval (CI), p-value after meta-analysis of classcompound1 against different microorganisms in Phylum stratification for 24-hours incubation. Finally, it shows the number of studies being used.

Hours	Number of studies	Phylum	Classcompound1	MIC	CI (low - upper boundary)	p-value
24	34	Bacillota	xanthohumol	21,881	10,438-33,323	0

24	7	Bacteroida	xanthohumol	39,429	27,795-51,062	0
24	35	Bacillota	xanthohumol	51,92	44,036-59,803	0
24	2	Actinomycetota	xanthohumol	46,875	16,251-77,499	0
24	3	Ascomycota	xanthohumol	50	30,4-69,6	0
24	23	Bacillota	humulone	40,848	22,824-58,871	0
24	25	Bacillota	lupulone	10,761	2,859-18,663	0
24	3	Ascomycota	lupulone	666,667	340,006-993,327	0

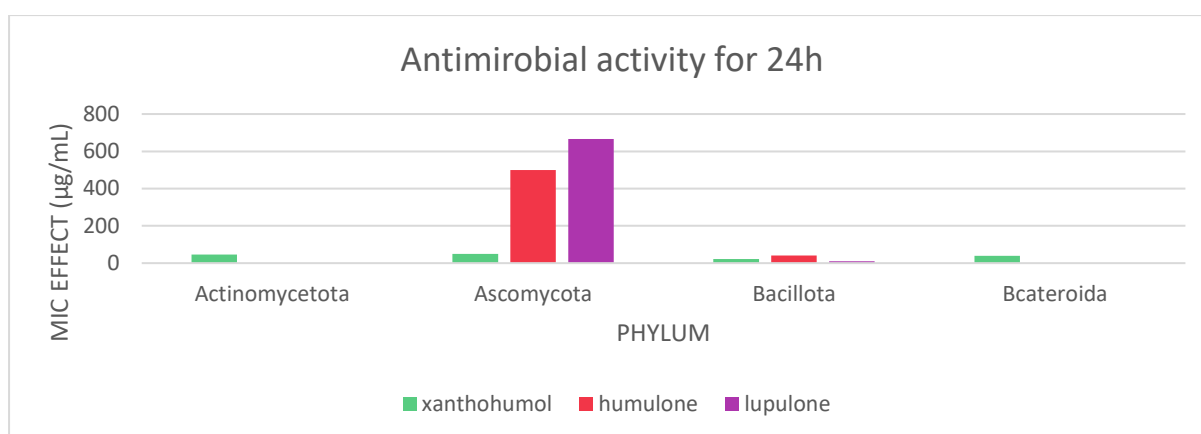


Figure 16: Minimum Inhibitory Concentration of meta-analysis of hop compounds after 24h incubation against microorganisms. Green stands for xanthohumol, pink for humulone and purple for lupulone.

Table 10: Results of meta-analysis process. The table illustrates MIC value along with Confidence Interval (CI), p-value after meta-analysis of classcompound1 against different microorganisms in Phylum stratification for 48-hours incubation. Finally, it shows the number of studies being used.

Hours	Number of studies	Phylum	Classcompound1	MIC	CI (low - upper boundary)	p-value
48	4	Ascomycota	humulone	500	153,524-846,476	0

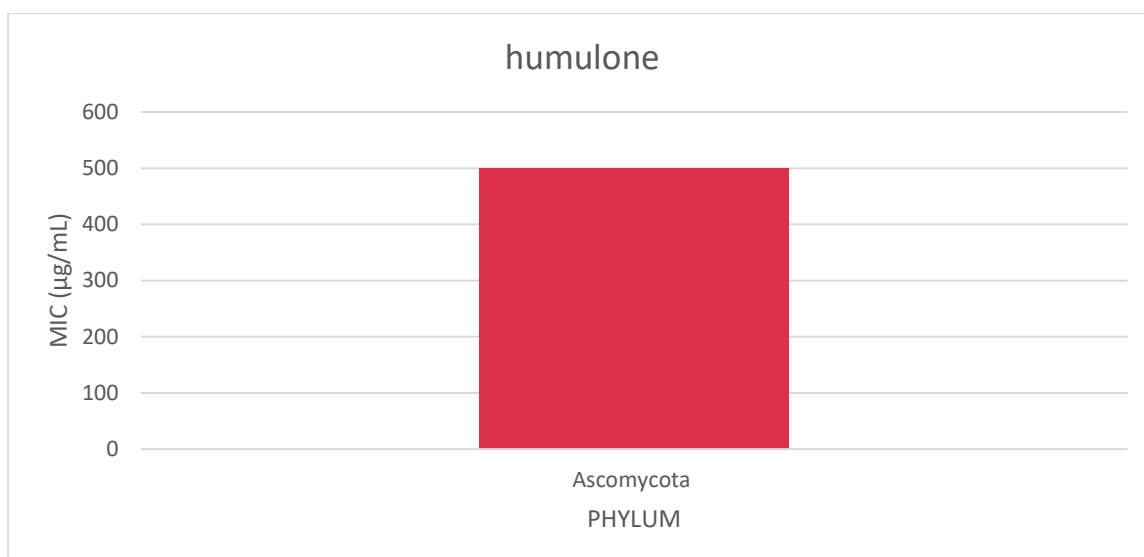


Figure 17: Minimum Inhibitory Concentration of meta-analysis of hop compounds after 48h incubation against different microorganisms. Red for humulone.

Table 11: Results of meta-analysis process. The table illustrates MIC value along with Confidence Interval (CI), p-value after meta-analysis of classcompound1 against different microorganisms in Phylum stratification for 24-hours incubation. Finally, it shows the number of studies being used.

Hours	Number of studies	Phylum	Classcompound1	MIC	CI (low - upper boundary)	p-value
24	4	Actinomycetota	CO2-extract	3,488	2,728-4,247	0,144
24	19	Bacillota	CO2-extract	377,531	58,671-696,391	0
24	14	Bacillota	Hydroacetic-extract	55,657	12,151-99,163	0
24	2	Actinomycetota	Hydralcoholic-extract	39	38,2-39,8	1
24	17	Bacillota	Hydralcoholic-extract	132,941	45,341-220,542	0
24	4	Pseudomonadota	Hydralcoholic-extract	625	624,434-625,566	1
24	3	Ascomycota	Hydralcoholic-extract	273,33	(-)-77,594-624,261	0

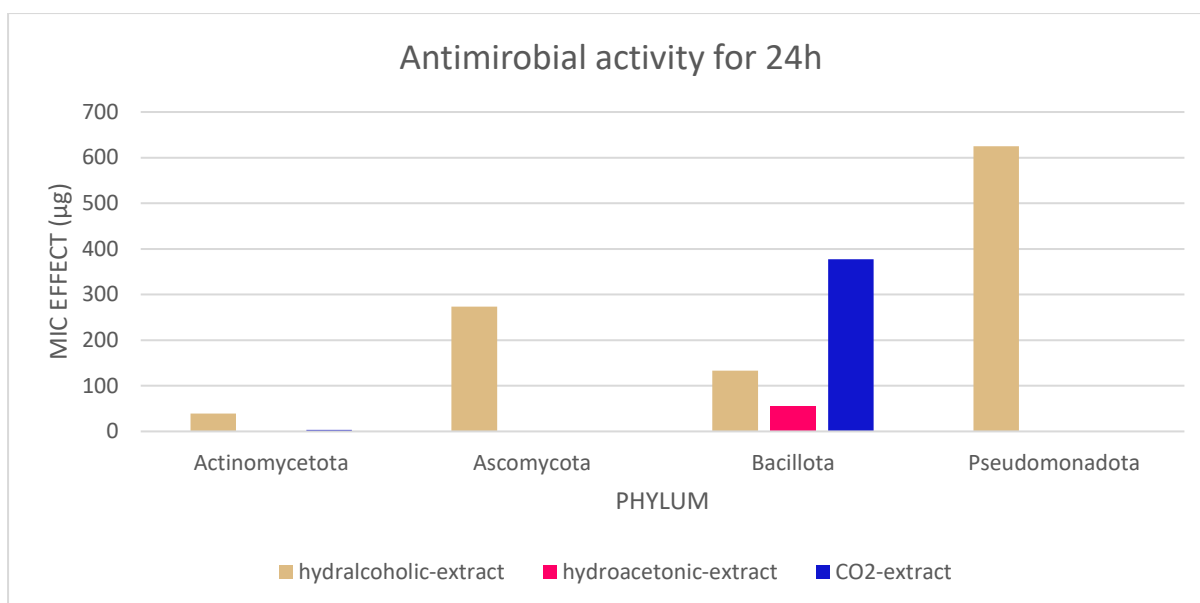


Figure 18: Minimum Inhibitory Concentration of meta-analysis of hop extracts after 24h incubation against microorganisms. Beige stands for hydraalcoholic-extract, blue for CO2-extract and pink for hydroacetonc-extract.

Table 12: Results of meta-analysis process. The table illustrates MIC value along with Confidence Interval (CI), p-value after meta-analysis of classcompound1 against different microorganisms in Phylum stratification for 48-hours incubation. Finally, it shows the number of studies being used.

Hours	Number of studies	Phylum	Classcompound1	MIC	CI (low - upper boundary)	p-value
48	19	Bacillota	CO2-extract	32,163	7,247-57,979	0
48	12	Pseudomonadota	CO2-extract	2604,167	1550,473-3657,86	0
48	4	Actinomycetota	CO2-extract	15,625	15,059-16,191	1
48	4	Ascomycota	CO2-extract	500	153,524-846,476	0
48	14	Bacillota	Hydroacetonc-extract	92,257	71,858-112,656	0
48	12	Actinomycetota	Hydraalcoholic-extract	154,667	109,761-199,572	0
48	24	Bacillota	Hydraalcoholic-extract	86,667	64,579-108,754	0
48	12	Fusobacteriota	Hydraalcoholic-extract	250,667	154,914-346,419	0
48	4	Ascomycota	Hydraalcoholic-extract	384	239,157-528,843	0

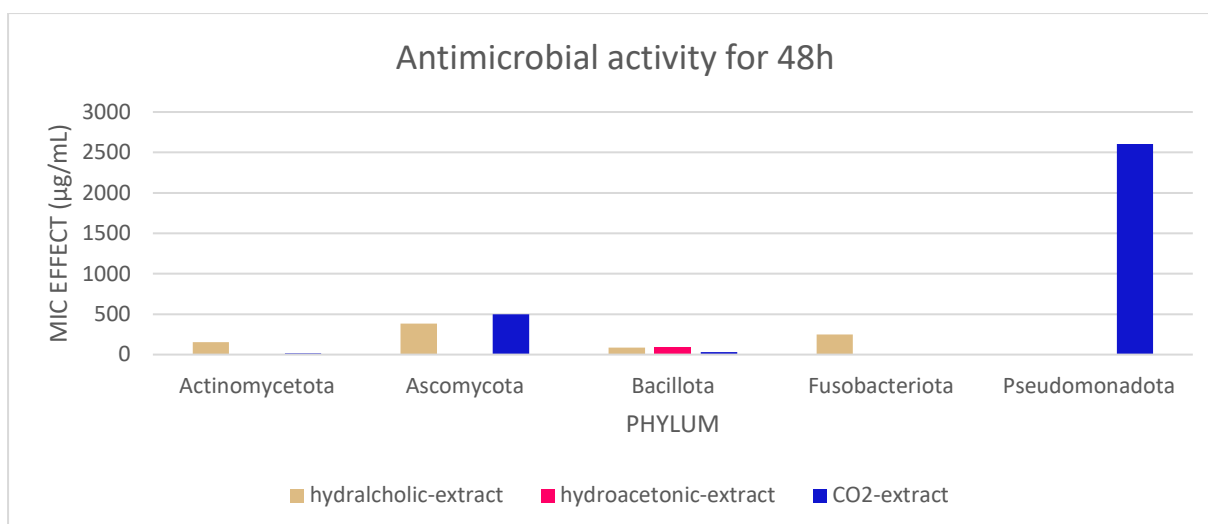


Figure 19: Minimum Inhibitory Concentration of meta-analysis of hop extracts after 48h incubation against different microorganisms. Beige stands for hydralcoholic-extract, blue for CO2-extract and pink for hydroacetic-extract.

In those diagrams, xanthohumol has the strongest antimicrobial activity against Ascomycota (MIC: 21,881 µg/mL), while lupulone has slightly better activity (MIC:10,761 µg/mL) than xanthohumol when referring to Bacillota in 24h incubation.

Against Bacillota in 24h incubation hydroacetic-extract seems to have better activity than the other two extracts (MIC: 55,657 µg/mL), while in contrast in 48h CO2-extract seems to have the strongest (MIC: 32,163 µg/mL) and hydroacetic-extract the weakest (MIC: 92,257 µg/mL).

3.3.1.3 By probiotic, food spoilage, pathogenicity

The diagrams here illustrate the meta-analysis of classcompound1 against the stratification of microorganisms in probiotic, pathogenicity and food spoilage activity.

Table 13: Results of meta-analysis process. The table illustrates MIC value along with Confidence Interval (CI), p-value after meta-analysis of classcompound1 against stratification of microorganisms in probiotic, pathogenic and food-spoilage for 24-hours incubation. Finally, it shows the number of studies being used.

Hours	Number of studies	Probiotic/ pathogenicity/ food-spoilage	Classcompound1	MIC	CI (low - upper boundary)	p-value
24	34	opportunistic pathogens	xanthohumol	21,881	10,438-33,323	0
24	23	opportunistic pathogens	humulone	40,848	22,824-58,871	0
24	25	opportunistic pathogens	lupulone	10,761	2,859-18,663	0

24	6	probiotic	xanthohumol	8,486	4,701-12,270	0
24	5	probiotic	humulone	5,009	0,969-9,049	0
24	6	probiotic	lupulone	4,927	2,706-7,148	0
24	28	food spoilage	xanthohumol	21,923	9,018-34,828	0
24	17	food spoilage	humulone	43,353	20,314-66,391	0
24	20	food spoilage	lupulone	12,402	2,661-22,143	0
24	23	opportunistic pathogens	CO2-extract	355,741	75,21-636,272	0
24	25	opportunistic pathogens	hydralcoholic-extract	220,08	119,665-320,495	0
24	14	opportunistic pathogens	hydroacetic-extract	55,657	12,151-99,163	0
24	2	probiotic	CO2-extract	502,50	(-)472,582-1477,582	0
24	12	food spoilage	CO2-extract	421,908	0,947-842,868	0
24	9	food spoilage	hydralcoholic-extract	53,667	32,422-74,912	0
24	14	food spoilage	hydroacetic-extract	55,657	12,151-99,163	0

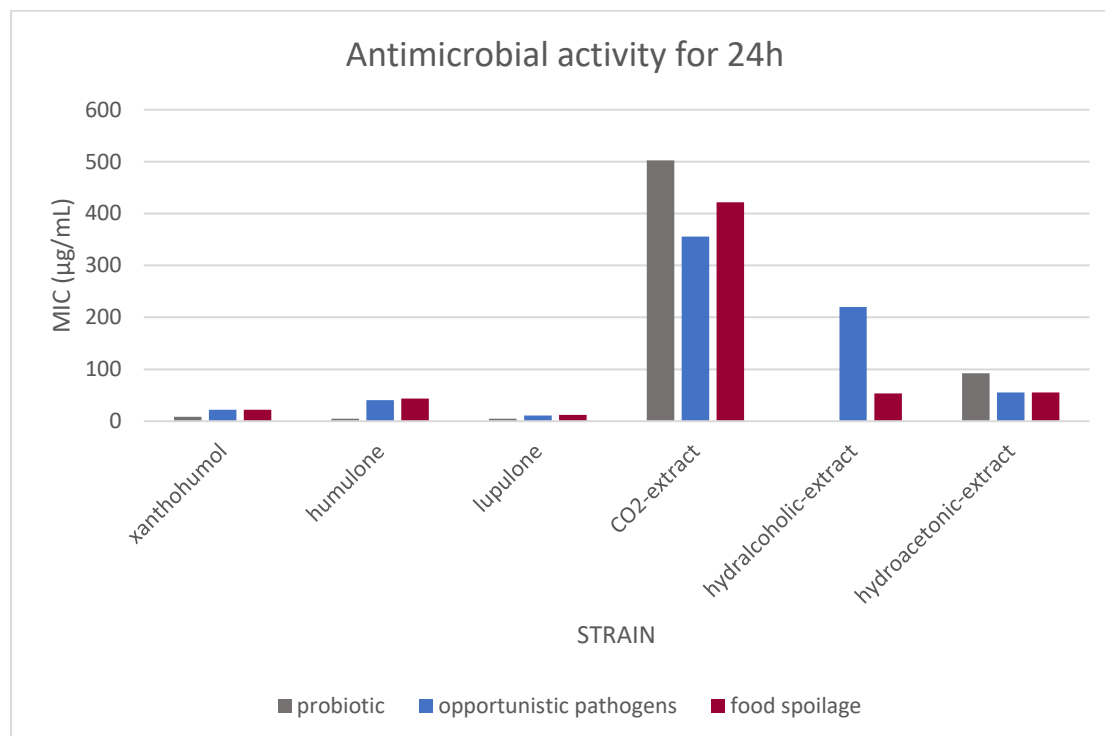


Figure 20: Minimum Inhibitory Concentration of meta-analysis of hop compounds and extracts after 24h incubation against different microorganisms after stratification in probiotic, pathogenic, food-spoilage. Grey stands for probiotic, blue for opportunistic pathogens and red for food spoilage.

Table 14: Results of meta-analysis process. The table illustrates MIC value along with Confidence Interval (CI), p-value after meta-analysis of classcompound1 against stratification of microorganisms in probiotic, pathogenic and food-spoilage for 48-hours incubation. Finally, it shows the number of studies being used.

Hours	Number of studies	Probiotic/ pathogenicity/ food-spoilage	Classcompound1	MIC	CI (low - upper boundary)	p-value
48	7	food spoilage	xanthohumol	23,455	8,763-38,146	0
48	7	food spoilage	humulone	700	271,78- 1128,22	0
48	45	opportunistic pathogens	xanthohumol	49,932	43,332- 56,532	0
48	2	opportunistic pathogens	humulone	375	130,005- 619,995	0
48	3	opportunistic pathogens	lupulone	503,334	(-)-21,392- 1028,059	0
48	7	probiotic	xanthohumol	39,429	27,795- 51,062	0
48	6	probiotic	catechin	950	428,996- 1471,004	0
48	31	food spoilage	CO2-extract	1028,053	448,059- 1608,047	0
48	24	food spoilage	hydralcoholic- extract	86,667	64,579- 108,754	0
48	14	food spoilage	hydroacetic- extract	92,257	71,858- 112,656	0
48	31	opportunistic pathogens	CO2-extract	550,23	105,87- 994,591	0
48	53	opportunistic pathogens	hydralcoholic- extract	169,66	131,083- 208,238	0
48	14	opportunistic pathogens	hydroacetic- extract	92,257	71,858- 112,656	0
48	18	probiotic	hydralcoholic- extract	149,333	115,699- 182,967	0
48	14	probiotic	hydroacetic- extract	92,257	71,858- 112,656	0

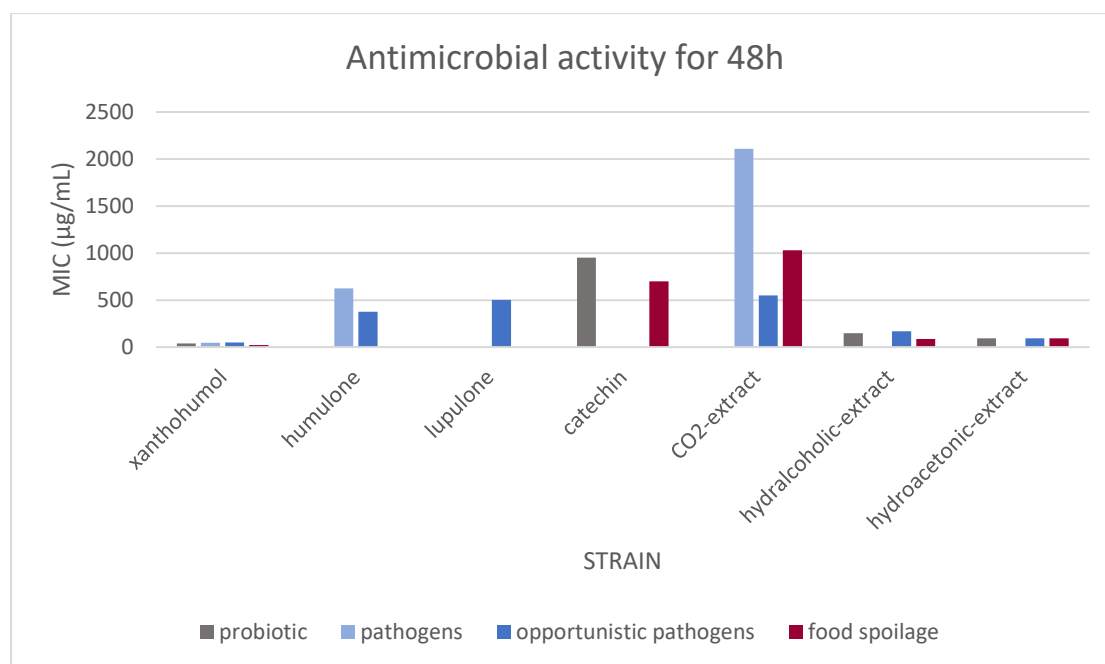


Figure 21: Minimum Inhibitory Concentration of meta-analysis of hop compounds and extracts after 48h incubation against different microorganisms after stratification in probiotic, pathogenic, food-spoilage. Grey stands for probiotic, blue for opportunistic pathogens, baby blue for pathogens and red for food spoilage.

In those diagrams we observe that for 24h incubation lupulone has the strongest antimicrobial activity, but for 48h incubation xanthohumol has the strongest one against probiotic, pathogenic and food spoilage microorganisms (lupulone MIC: 4,93 µg/mL, 10,76 µg/mL, 12,4 µg/mL respectively and xanthohumol MIC: 39,43 µg/mL, 45 µg/mL, 49,93 µg/mL, 23,46 µg/mL). One important feature is that at the 24h incubation there is not presence of pathogenic microorganisms.

Referring to 24h incubation hydroacetic-extract seems to have in almost every category better activity than other hop extracts (MIC: 92,26 µg/mL, 55,66 µg/mL, 55,66 µg/mL respectively.) In 48h incubation as well, hydroacetic-extract seems to have better activity than the other extracts, like in 24h with MIC values, in all three categories, probiotic, opportunistic pathogens, food spoilage, except pathogens where there is no data, and the value is equal to 92,25 µg/mL.

3.3.2 Results of meta-analysis in classcompound2

3.3.2.1 By strain

The diagrams here illustrate the meta-analysis of classcompound2 against the stratification of microorganisms in strains.

Table 15: Results of meta-analysis process. The table illustrates MIC value along with Confidence Interval (CI), p-value after meta-analysis of classcompound2 against different strains for 24-hours incubation. Finally, it shows the number of studies being used.

Hours	Number of studies	Strain	Classcompound2	MIC	CI (low - upper boundary)	p-value
24	3	Staphylococcus epidermidis	chalcones	1,366	0,123-2,609	0,027
24	15	Staphylococcus aureus	chalcones	13,609	6,412-20,806	0
24	3	Bacillus subtilis	chalcones	7	1,12-12,88	0
24	3	Bacillus megaterium	chalcones	10	9,2-10,8	1
24	3	Streptococcus salivarius	chalcones	23,333	10,267-36,4	0
24	3	Streptococcus saprophyticus	chalcones	2,333	1,027-3,64	0,069
24	6	Streptococcus aureus	chalcones	70,083	29,806-110,361	0
24	2	Enterococcus faecalis	chalcones	62	61,307-62,693	1
24	2	Staphylococcus epidermidis	α -acids	18,75	(-)3,3-40,8	0
24	12	Staphylococcus aureus	α -acids	146,75	82,284-211,216	0
24	9	Bacillus subtilis	α -acids	119,556	(-)94,537-333,648	0
24	3	Streptococcus saprophyticus	α -acids	5,308	1,196-9,421	0
24	2	Enterococcus faecalis	α -acids	60	59,307-60,693	1
24	2	Staphylococcus epidermidis	β -acids	2,25	(-)1,18-5,68	0
24	13	Staphylococcus aureus	β -acids	18,51	2,477-34,542	0
24	3	Bacillus subtilis	β -acids	2,333	1,027-3,64	0
24	3	Bacillus megaterium	β -acids	7,667	3,093-12,24	0
24	3	Streptococcus salivarius	β -acids	68,333	6,268-130,399	0
24	3	Streptococcus saprophyticus	β -acids	2,333	1,027-3,64	0,069

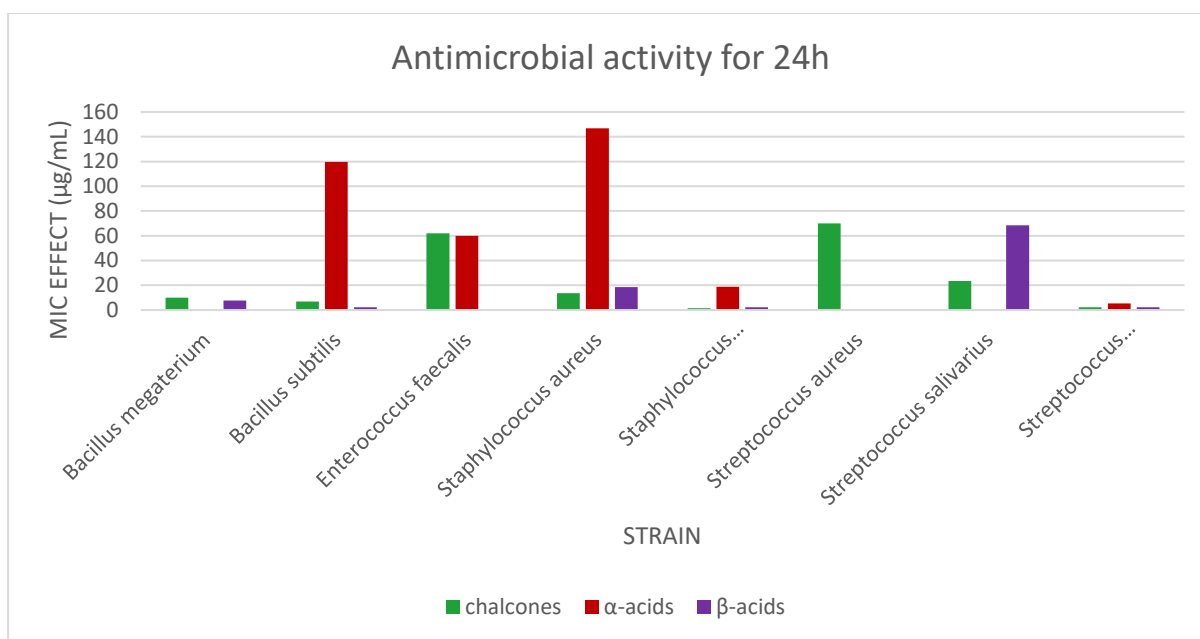


Figure 22: Minimum Inhibitory Concentration of meta-analysis of hop compounds' classes against microorganisms after 24h incubation. Green stands for chalcones, red for α-acids and purple for β-acids.

Table 16: Results of meta-analysis process. The table illustrates MIC value along with Confidence Interval (CI), p-value after meta-analysis of classcompound2 against different strains for 24-hours incubation. Finally, it shows the number of studies being used.

Hours	Number of studies	Strain	Classcompound2	MIC	CI (low - upper boundary)	p-value
24	4	Propionibacterium acnes	CO2-extract	3,488	2,728-4,247	0,144
24	6	Staphylococcus aureus	CO2-extract	6,32	2,205-10,425	0
24	2	Listeria monocytogenes	CO2-extract	10	9,307-10,693	1
24	2	Staphylococcus epidermidis	CO2-extract	0,098	(-)0,702-0,898	1
24	4	Streptococcus aureus	CO2-extract	1666,667	1013,345-2319,988	0
24	3	Enterococcus faecalis	CO2-extract	696,667	(-)580,689-1974,023	0
24	2	Enterococcus faecalis	hydralcoholic-extract	50,502	27,962-73,041	0
24	2	Staphylococcus aureus	hydralcoholic-extract	39	38,2-39,8	1
24	2	Staphylococcus epidermidis	hydralcoholic-extract	68,5	10,681-126,319	0
24	2	Staphylococcus lugdunensis	hydralcoholic-extract	390,5	(-)69,112-850,112	0

24	2	Staphylococcus warneri	hydralcoholic-extract	332	(-)242,269-906,269	0
24	2	Streptococcus agalactiae	hydralcoholic-extract	58,5	20,281-96,719	0
24	2	Pseudomonas aeruginosa	hydralcoholic-extract	625	624,2-625,8	1
24	3	Candida albicans	hydralcoholic-extract	273,333	(-)77,594-624,261	0
24	3	Streptococcus aureus	hydralcoholic-extract	62,333	0,921=123,746	0
24	14	Staphylococcus aureus	hydroacetic-extract	55,657	12,151-99,163	0

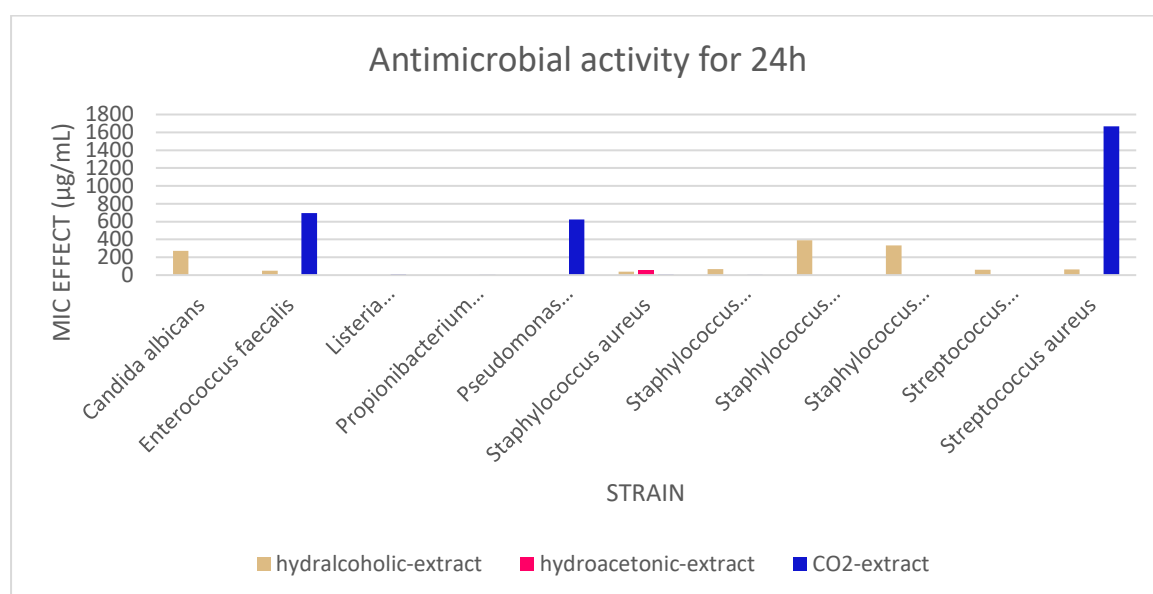


Figure 23: Minimum Inhibitory Concentration of meta-analysis of hop extracts against microorganisms after 24h incubation. Beige stands for hydralcoholic-extracts, blue for CO2-extract, pink for hydroacetic-extract.

Table 17: Results of meta-analysis process. The table illustrates MIC value along with Confidence Interval (CI), p-value after meta-analysis of classcompound2 against different strains for 48-hours incubation. Finally it shows the number of studies being used.

Hours	Number of studies	Strain	Classcompound2	MIC	CI (low - upper boundary)	p-value
48	3	Staphylococcus aureus	chalcones	5,167	3,138-7,195	0
48	3	Listeria monocytogenes	chalcones	6,233	0,092-12,375	0
48	3	Escherichia coli	chalcones	200	199,434-200,566	1
48	3	Salmonella enterica	chalcones	200	199,434-200,566	1

48	7	Bacteroides fragilis	chalcones	39,429	27,795-51,062	0
48	5	Clostridium perfringens	chalcones	32,6	18,719-46,481	0
48	28	Clostridium difficile	chalcones	59,036	51,644-66,428	0
48	2	Propionibacterium acnes	chalcones	46,875	16,251-77,499	0
48	3	Bacillus subtilis	flavonols	1200	569,96-1830,04	0
48	2	Pseudomonas fluorescens	flavonols	1700	1699,2-1700,8	0
48	7	Bacteroides fragilis	α -acids	767,143	408,979-1125,307	0
48	5	Clostridium perfringens	α -acids	1062	808,459-1315,541	0
48	28	Clostridium difficile	α -acids	737,143	604,151-870,135	0
48	7	Bacteroides fragilis	β -acids	258,571	168,102-349,041	0
48	5	Clostridium perfringens	β -acids	198	161,123-234,877	0
48	28	Clostridium difficile	β -acids	38,857	47,32-63,64	0

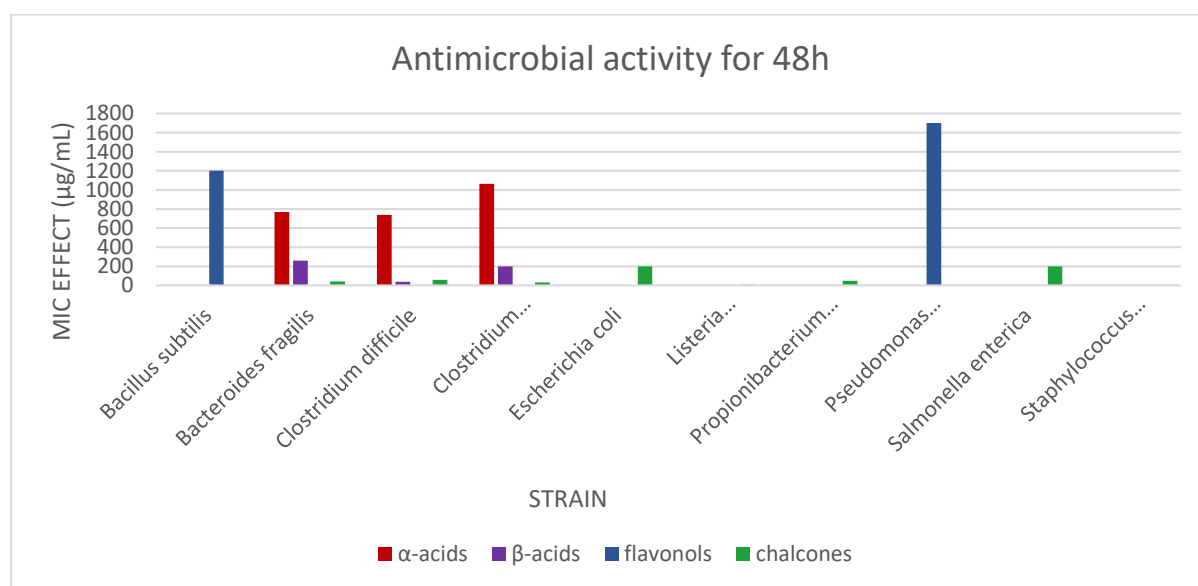


Figure 24: Minimum Inhibitory Concentration of meta-analysis of hop compounds' classes against microorganisms after 48h incubation. Red stands for α -acids, purple for β -acids, blue for flavonols and green for chalcones.

Table 18: Results of meta-analysis process. The table illustrates MIC value along with Confidence Interval (CI), p-value after meta-analysis of classcompound2 against different strains for 48-hours incubation. Finally, it shows the number of studies being used.

Hours	Number of studies	Strain	Classcompound2	MIC	CI (low - upper boundary)	p-value
48	7	Staphylococcus aureus	CO2-extract	46,429	(-)6,222-99,080	0
48	7	Listeria monocytogenes	CO2-extract	37,186	(-)16,563-90,934	0
48	6	Escherichia coli	CO2-extract	2604,167	1041,287-4167,047	0
48	6	Salmonella enterica	CO2-extract	2604,167	1041,287-4167,047	0
48	2	Streptococcus mutans	CO2-extract	0,391	(-)0,409-1,191	1
48	2	Streptococcus sanguinis	CO2-extract	0,781	(-)0,019-1,581	1
48	4	Propionibacterium acnes	CO2-extract	15,63	15,059-16,191	1
48	6	Bifidobacterium dentium	hydralcoholic-extract	213,333	160,444-266,223	0
48	6	Bifidobacterium longum	hydralcoholic-extract	96	67,951-124,049	0
48	6	Lactobacillus salivarius	hydralcoholic-extract	138,667	88,138-189,016	0
48	6	Streptococcus mutans	hydralcoholic-extract	106,667	80,222-133,111	0
48	6	Streptococcus salivarius	hydralcoholic-extract	34,667	22,079-47,254	0
48	6	Streptococcus sobrinus	hydralcoholic-extract	66,667	38,135-95,198	0
48	12	Fusobacterium nucleatum	hydralcoholic-extract	250,667	154,914-346,419	0
48	4	Candida albicans	hydralcoholic-extract	384	239,157-528,843	0
48	14	Lactobacillus acidophilus	hydroacetic-extract	92,257	71,858-112,656	0

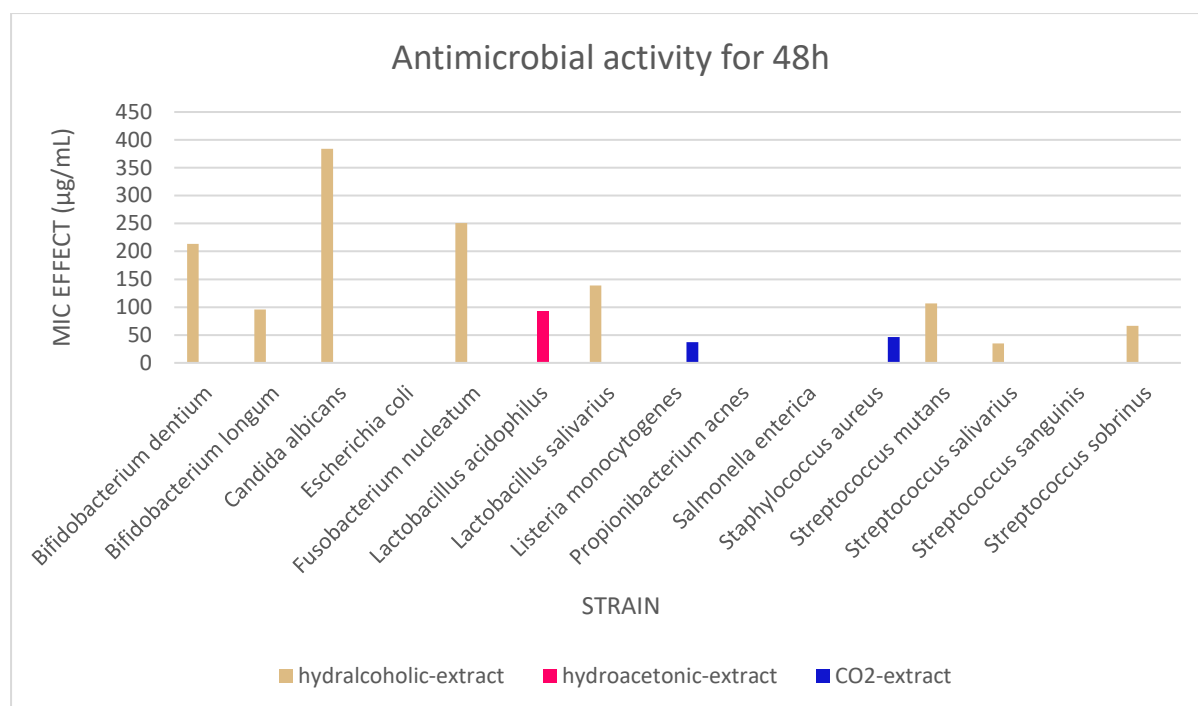


Figure 25: Minimum Inhibitory Concentration of meta-analysis of hop extracts against microorganisms after 48h incubation. Beige stands for hydralcoholic-extract, blue for CO2-extract and pink for hydroacetonc-extract.

As we can observe, during 24h incubation in *Bacillus subtilis* β -acids (MIC:2,333 $\mu\text{g/mL}$) have stronger antimicrobial activity than from chalcones and α -acids, while in *Staphylococcus aureus* and *Staphylococcus epidermidis* chalcones have better MIC values 13,609 $\mu\text{g/mL}$, 1,366 $\mu\text{g/mL}$ correspondingly than to α and β -acids.

In 48h incubation of compounds class2, chalcones against *Clostridium perfringens* have MIC equal to 32,6 $\mu\text{g/mL}$, α -acids have 1062 $\mu\text{g/mL}$ and β -acids 198 $\mu\text{g/mL}$, resulting in chalcones to be the best one, same as *Bacteroides fragilis*.

CO2-extract has MIC value against *Staphylococcus aureus* in 24h equal to 6,32 $\mu\text{g/mL}$, while in hydralcoholic and hydroacetonc extract the value is approximately the same , 39 $\mu\text{g/mL}$ and 55,657 $\mu\text{g/mL}$ correspondingly, thus CO2-extract has the best activity.

Both in *Enterococcus faecalis* and in *Streptococcus aureus* in 24h incubation with etxtracts, hydralcoholic extract (MIC: 50,502 $\mu\text{g/mL}$, 62,333 $\mu\text{g/mL}$) has better activity than CO2-extract (MIC: 696,667 $\mu\text{g/mL}$, 1666,667 $\mu\text{g/mL}$). In 48h the only data been significant is that CO2-extract against *Streptococcus mutans* (MIC: 0,391 $\mu\text{g/mL}$) has better activity than in hydralcoholic-extract (MIC: 106,667 $\mu\text{g/mL}$).

3.3.2.2 By phylum

The diagrams here illustrate the meta-analysis of classcompound2 against the stratification of microorganisms in Phylum.

Table 19: Results of meta-analysis process. The table illustrates MIC value along with Confidence Interval (CI), p-value after meta-analysis of classcompound2 against different microorganisms in Phylum stratification for 24-hours incubation. Finally, it shows the number of studies being used.

Hours	Number of studies	Phylum	Classcompound2	MIC	CI (low - upper boundary)	p-value
24	39	Bacillota	chalcones	22,635	12,419-32,852	0
24	32	Bacillota	α -acids	96,578	6,035-187,122	0

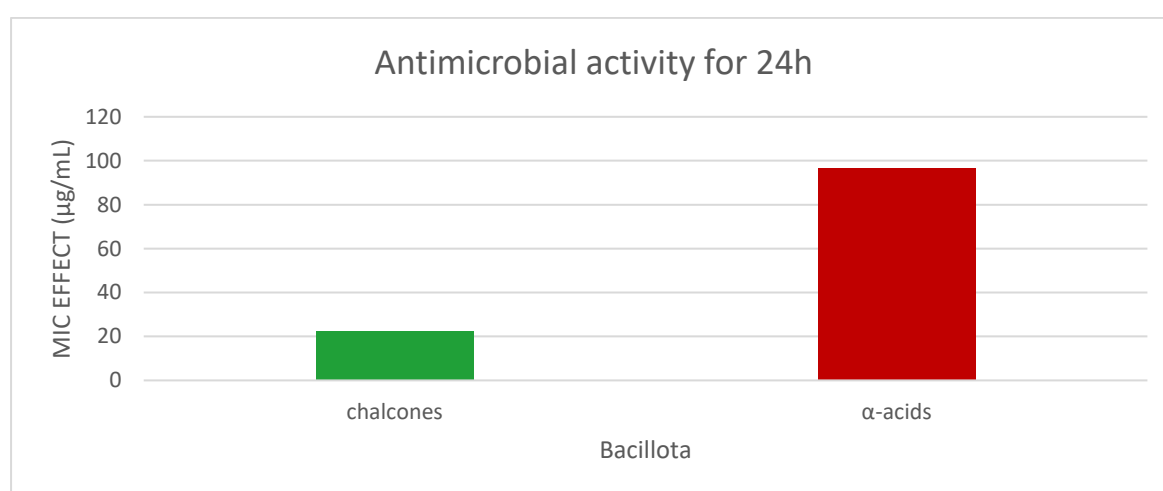


Figure 26: Minimum Inhibitory Concentration of meta-analysis of hop compounds' classes against Bacillota after 24h incubation. Green stands for chalcones and red for α -acids.

Table 20: Results of meta-analysis process. The table illustrates MIC value along with Confidence Interval (CI), p-value after meta-analysis of classcompound2 against different microorganisms in Phylum stratification for 24-hours incubation. Finally, it shows the number of studies being used.

Hours	Number of studies	Phylum	Classcompound2	MIC	CI (low - upper boundary)	p-value
24	4	Actinomycetota	CO2-extract	3,488	2,728-4,247	0,144
24	19	Bacillota	CO2-extract	377,531	58,671-696,391	0
24	2	Actinomycetota	hydralcoholic-extract	39	38,2-39,8	1
24	17	Bacillota	hydralcoholic-extract	132,941	45,341-220,542	0
24	4	Pseudomonadota	hydralcoholic-extract	625	624,434-625,566	1

24	3	Ascomycota	hydralcoholic-extract	273,333	(-)77,594-624,261	0
24	14	Bacillota	hydroacetonic-extract	55,657	12,151-99,163	0

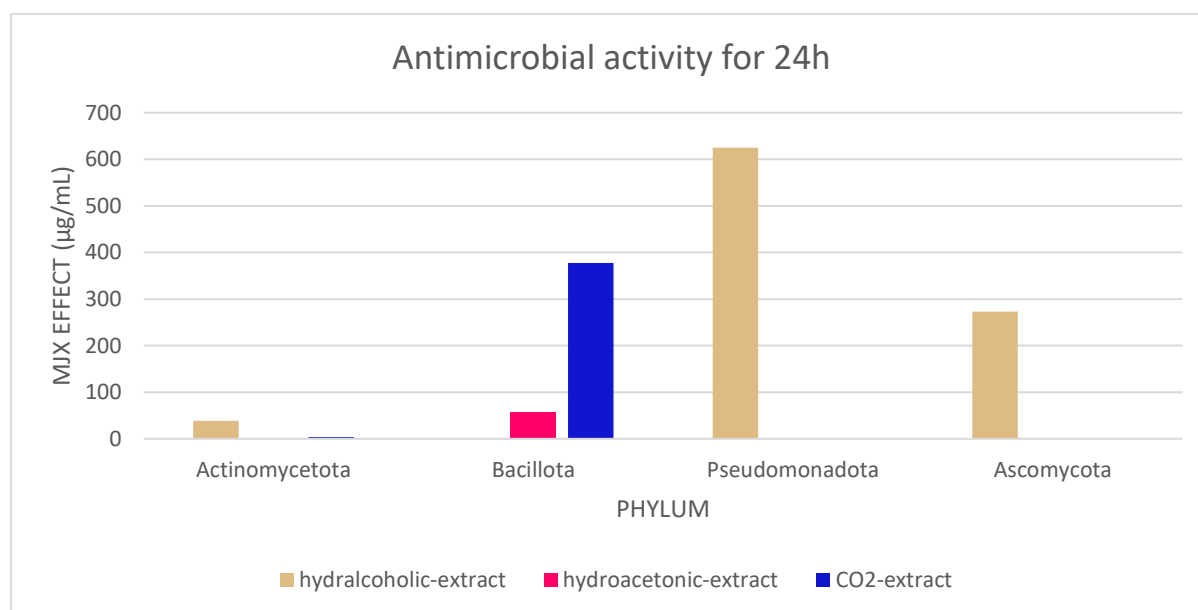


Figure 27: Minimum Inhibitory Concentration of meta-analysis of hop extracts against microorganisms' classes after 24h incubation. Beige stands for hydralcoholic-extract, blue for CO₂-extract and pink for hydroacetonic-extract.

Table 21: Results of meta-analysis process. The table illustrates MIC value along with Confidence Interval (CI), p-value after meta-analysis of classcompound2 against different microorganisms in Phylum stratification for 48-hours incubation. Finally it shows the number of studies being used.

Hours	Number of studies	Phylum	Classcompound2	MIC	CI (low - upper boundary)	p-value
48	41	Bacillota	chalcones	45,156	36,677-53,634	0
48	6	Pseudomonadota	chalcones	200	199,6-200,4	1
48	7	Bacteroida	chalcones	39,429	27,795-51,062	0
48	2	Actinomycetota	chalcones	46,875	16,251-77,499	0
48	3	Ascomycota	chalcones	50	30,4-69,6	0
48	7	Bacteroida	α-acids	767,143	408,979-1125,307	0
48	33	Bacillota	α-acids	768,364	661,831-910,896	0

48	4	Ascomycota	α -acids	500	153,524-846,476	0
48	30	Bacillota	β -acids	16,786	7,581-25,992	0
48	11	Bacillota	flavonols	748	357,12-1138,88	0
48	2	Pseudomonadota	flavonols	1700	1699,2-1700,8	1

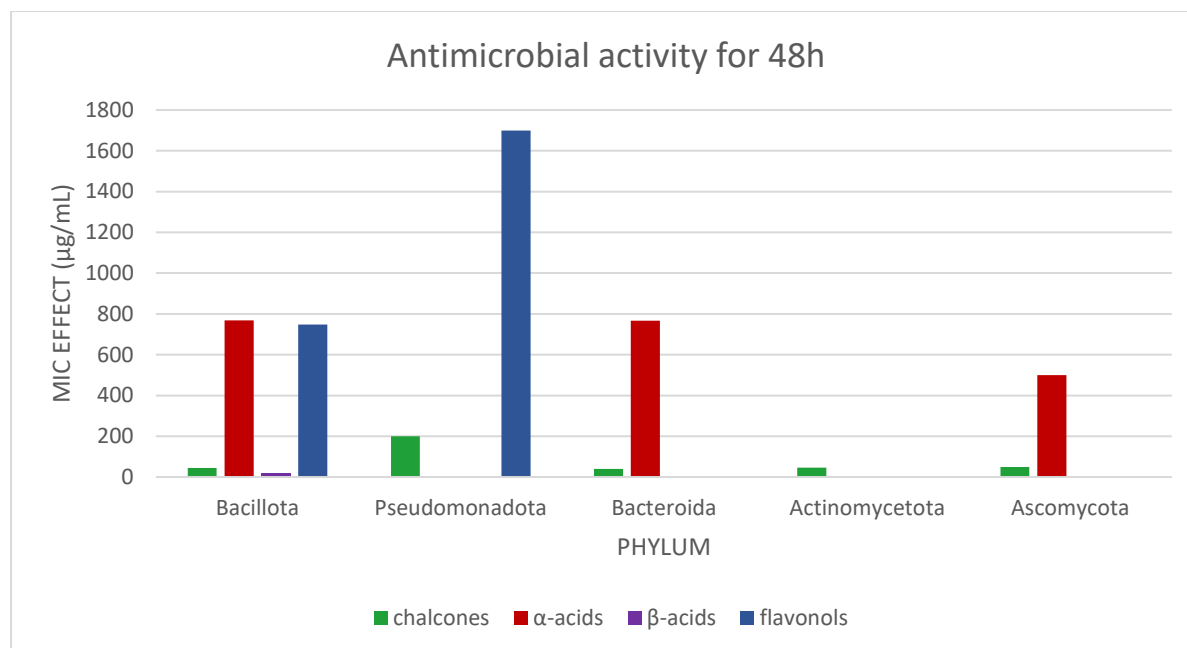


Figure 28: Minimum Inhibitory Concentration of meta-analysis of hop compounds' classes against microorganisms' classes after 48h incubation. Red stands for α -acids, purple for β -acids, blue for flavonols and green for chalcones.

Table 22: Results of meta-analysis process. The table illustrates MIC value along with Confidence Interval (CI), p-value after meta-analysis of classcompound2 against different microorganisms in Phylum stratification for 48-hours incubation. Finally, it shows the number of studies being used.

Hours	Number of studies	Phylum	Classcompound2	MIC	CI (low - upper boundary)	p-value
48	19	Bacillota	CO2-extract	32,613	7,247-57,979	0
48	12	Pseudomonadota	CO2-extract	2604,167	1550,473-3657,86	0
48	4	Actinomycetota	CO2-extract	15,625	15,059-16,191	1
48	4	Ascomycota	CO2-extract	500	153,524-846,476	0
48	12	Actinomycetota	hydralcoholic-extract	154,667	109,761-199,572	0

48	24	Bacillota	hydralcoholic-extract	86,667	64,579-108,754	0
48	12	Fusobacteriota	hydralcoholic-extract	250,667	154,914-346,419	0
48	4	Ascomycota	hydralcoholic-extract	384	239,157-528,843	0
48	14	Bacillota	hydroacetonc-extract	92,257	71,858-112,656	0

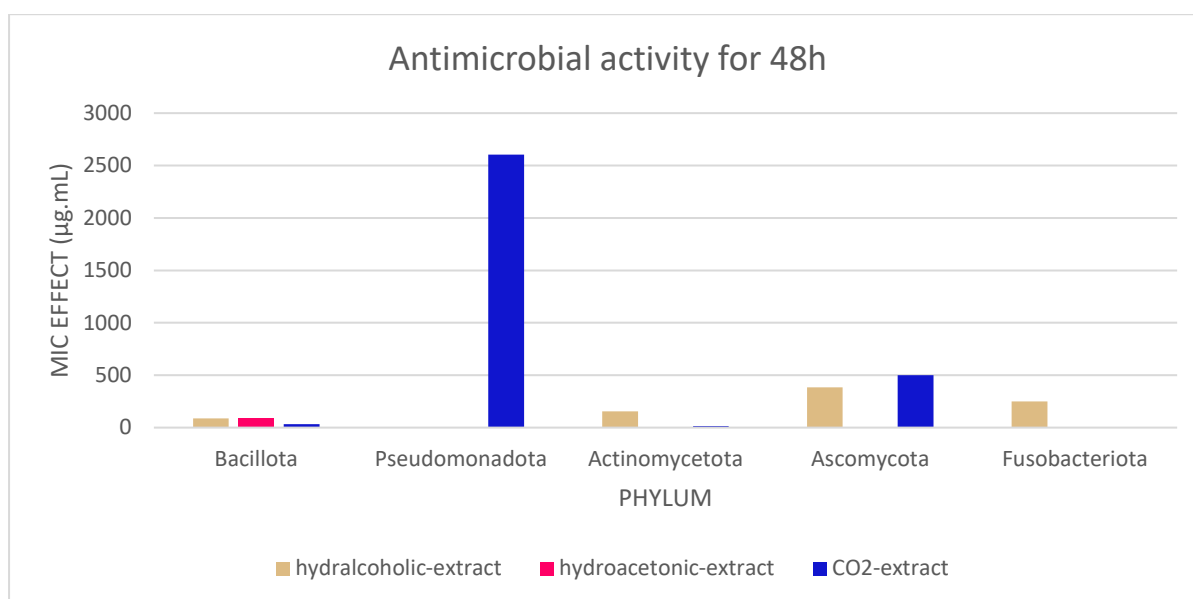


Figure 29: Minimum Inhibitory Concentration of meta-analysis of hop extracts against microorganisms after 48h incubation. Beige stands for hydralcoholic-extract, blue for CO2-extract and pink for hydroacetonc-extract.

To be more specific, Bacillota in 24h incubation have not so many data, but in 48h we can observe that β -acids have 16,786 $\mu\text{g/mL}$ MIC value, chalcones have 45,156 $\mu\text{g/mL}$ and α -acids and flavonols approximately the same values, resulting in β -acids as the best one in those conditions. Despite the few data against Bacteroida and Ascomycota among chalcones and α -acids, the first ones seem to have better activity, with MIC value equal to 39,429 $\mu\text{g/mL}$ and 767,143 $\mu\text{g/mL}$ respectively, in contrast with the latest with values 50 $\mu\text{g/mL}$ and 500 $\mu\text{g/mL}$.

CO2-extract against Bacillota in 24h are weakest (MIC: 377,531 $\mu\text{g/mL}$) than in hydroacetonc-extract (MIC: 55,657 $\mu\text{g/mL}$), an observation which is not the same in 48h incubation when the strongest is the CO2-extract with MIC value 32,613 $\mu\text{g/mL}$ in contrast with the hydralcoholic-extract with value equal to 86,667 $\mu\text{g/mL}$ and hydroacetonc-extract equal to 92,257 $\mu\text{g/mL}$.

3.3.2.3 By probiotic, food spoilage, pathogenicity

The diagrams here illustrate the meta-analysis of classcompound2 against the stratification of microorganisms into probiotic, opportunistic pathogens and food spoilage activity.

Table 23: Results of meta-analysis process. The table illustrates MIC value along with Confidence Interval (CI), p-value after meta-analysis of classcompound2 against stratification of microorganisms in probiotic, pathogenic and food-spoilage for 24-hours incubation. Finally it shows the number of studies being used.

Hours	Number of studies	probiotic/ food spoilage/ pathogenic	Classcompound2	MIC	CI (low - upper boundary)	p-value
24	33	food spoilage	chalcones	22,808	11,54-34,077	0
24	26	food spoilage	α -acids	111,077	5,464-216,69	0
24	25	food spoilage	β -acids	19,304	8,413-30,194	0
24	39	opportunistic pathogens	chalcones	22,635	12,419-32,825	0
24	32	opportunistic pathogens	α -acids	96,578	6,035-187,122	0
24	30	opportunistic pathogens	β -acids	16,786	7,581-25,992	0
24	6	probiotic	chalcones	8,486	4,701-12,27	0
24	10	probiotic	α -acids	108,1	(-)-93,479-309,679	0
24	6	probiotic	β -acids	4,927	2,706-7,148	0
24	12	food spoilage	CO2-extract	421,908	0,947-842,868	0
24	9	food spoilage	hydralcoholic-extract	53,667	32,422-74,912	0
24	14	food spoilage	hydroacetic-extract	55,657	12,151-99,163	0
24	23	opportunistic pathogens	CO2-extract	355,741	75,21-636,272	0
24	25	opportunistic pathogens	hydralcoholic-extract	220,08	119,665-320,495	0
24	14	opportunistic pathogens	hydroacetic-extract	55,657	12,151-99,163	0
24	2	probiotic	CO2-extract	502,5	(-)-472,582-1477,582	0

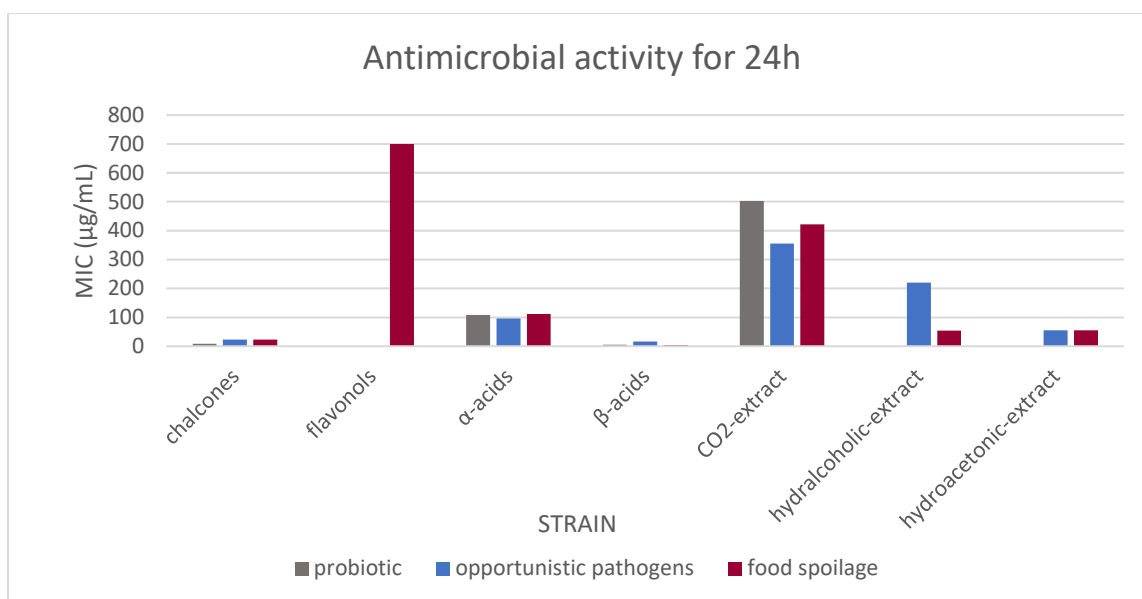


Figure 30: Minimum Inhibitory Concentration of meta-analysis of hop compounds and extracts after 24h incubation against different microorganisms after stratification in probiotic, pathogenic, food-spoilage. Grey stands for probiotic, blue for opportunistic pathogens, baby blue for pathogens and red for food spoilage.

Table 24: Results of meta-analysis process. The table illustrates MIC value along with Confidence Interval (CI), p-value after meta-analysis of classcompound2 against stratification of microorganisms in probiotic, pathogenic and food-spoilage for 48-hours incubation. Finally it shows the number of studies being used.

Hours	Number of studies	probiotic/ food spoilage/ pathogenic	Classcompound2	MIC	CI (low - upper boundary)	p-value
48	19	food spoilage	chalcones	73,599	33,272-113,925	0
48	5	food spoilage	α-acids	1062	808,459-1315,541	0
48	6	food spoilage	β-acids	166,668	109,57-223,765	0
48	5	pathogenic	chalcones	138	63,007-212,993	0
48	2	pathogenic	α-acids	625	(-)109,986-1359,986	0
48	15	opportunistic pathogens	flavonols	1001,867	662,973-1340,76	0
48	54	opportunistic pathogens	chalcones	53,354	41,631-65,078	0
48	42	opportunistic pathogens	α-acids	763,571	647,723-879,42	0
48	43	opportunistic pathogens	β-acids	125,535	70,982-180,088	0

48	7	probiotic	chalcones	39,429	27,795-51,062	0
48	6	probiotic	flavonols	950	428,996-1471,004	0
48	7	probiotic	α -acids	767,143	408,979-1125,307	0
48	7	probiotic	β -acids	258,571	168,102-349,041	0
48	31	food spoilage	CO2-extract	1028,053	448,059-1608,047	0
48	24	food spoilage	hydralcoholic-extract	86,667	64,579-108,754	0
48	8	pathogenic	CO2-extract	2109,375	793,746-3425,004	0
48	31	opportunistic pathogens	CO2-extract	550,23	105,87-994,591	0
48	53	opportunistic pathogens	hydralcoholic-extract	169,66	131,083-208,238	0
48	14	opportunistic pathogens	hydroacetic-extract	92,257	71,858-112,656	0
48	18	probiotic	hydralcoholic-extract	149,333	115,699-182,967	0
48	14	probiotic	hydroacetic-extract	92,257	71,858-112,656	0

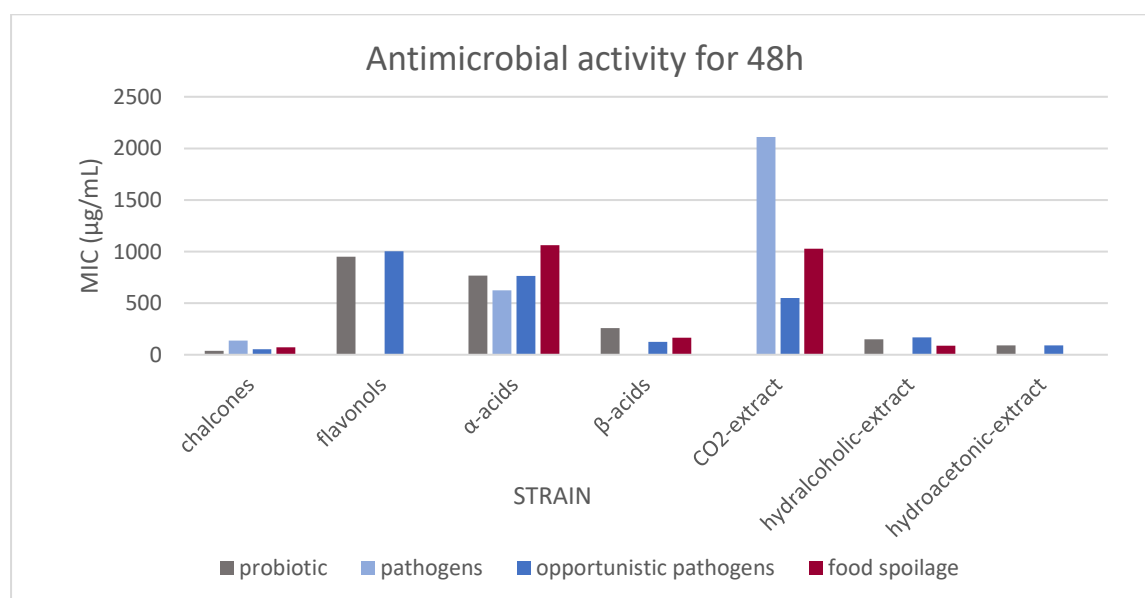


Figure 31: Minimum Inhibitory Concentration of meta-analysis of hop compounds and extracts after 48h incubation against different microorganisms after stratification in probiotic, pathogenic, food-spoilage. Grey stands for probiotic, blue for opportunistic pathogens, baby blue for pathogens and red for food spoilage.

On those diagrams we observe that in 24h incubation β -acids against probiotic, opportunistic pathogens and food spoilage have the best antimicrobial activity (MIC: 8,49 $\mu\text{g/mL}$, 22,64 $\mu\text{g/mL}$, 22,8 $\mu\text{g/mL}$ respectively) being followed by chalcones (MIC: 8,49 $\mu\text{g/mL}$, 22,64 $\mu\text{g/mL}$, 22,8 $\mu\text{g/mL}$ respectively). Although not all extracts gave us data, from the current data, hydroacetic-extract seems to have the best antimicrobial activity.

In 48h incubation, chalcones seems to have the best antimicrobial activity against probiotic, pathogens, opportunistic pathogens and food spoilage because their MIC values are equal to 39,43 $\mu\text{g/mL}$, 138 $\mu\text{g/mL}$, 53,35 $\mu\text{g/mL}$, 53,6 $\mu\text{g/mL}$. Same as before, hydroacetic-extract has the best antimicrobial activity from all other extracts.

3.3.3 Results of meta-analysis in classcompound3

3.3.3.1 By strain

The diagrams here illustrate the meta-analysis of classcompound3 against the stratification of microorganisms in strains.

Table 25: Results of meta-analysis process. The table illustrates MIC value along with Confidence Interval (CI), p-value after meta-analysis of classcompound3 against different strains for 24-hours incubation. Finally, it shows the number of studies being used.

Hours	Number of studies	Strain	Classcompound3	MIC	CI (low - upper boundary)	p-value
24	3	Staphylococcus epidermidis	flavonoids	1,366	0,123-2,609	0,027
24	15	Staphylococcus aureus	flavonoids	13,609	6,412-20,806	0
24	3	Bacillus subtilis	flavonoids	7	1,12-12,88	0
24	3	Bacillus megaterium	flavonoids	10	9,2-10,8	1
24	3	Streptococcus salivarius	flavonoids	23,333	10,267-36,4	0
24	3	Streptococcus saprophyticus	flavonoids	2,333	1,027-3,64	0,069
24	6	Streptococcus aureus	flavonoids	70,083	29,806-110,361	0
24	2	Enterococcus faecalis	flavonoids	62	61,307-62,692	1
24	4	Staphylococcus epidermidis	bitter acids	10,5	(-)2,544-23,544	0
24	2	Staphylococcus capitis	bitter acids	7,75	(-)6,46-21,96	0

24	25	Staphylococcus aureus	bitter acids	80,065	40,134-119,996	0
24	12	Bacillus subtilis	bitter acids	90,25	(-)75,015-255,515	0
24	4	Bacillus megaterium	bitter acids	7	3,512-10,488	0
24	4	Streptococcus salivarius	bitter acids	58,75	11,013-106,487	0
24	6	Streptococcus saprophyticus	bitter acids	3,825	1,706-5,943	0
24	3	Enterococcus faecalis	bitter acids	45	15,601-74,399	0
24	2	Staphylococcus haemolyticus	bitter acids	15,5	(-)12,919-43,919	0

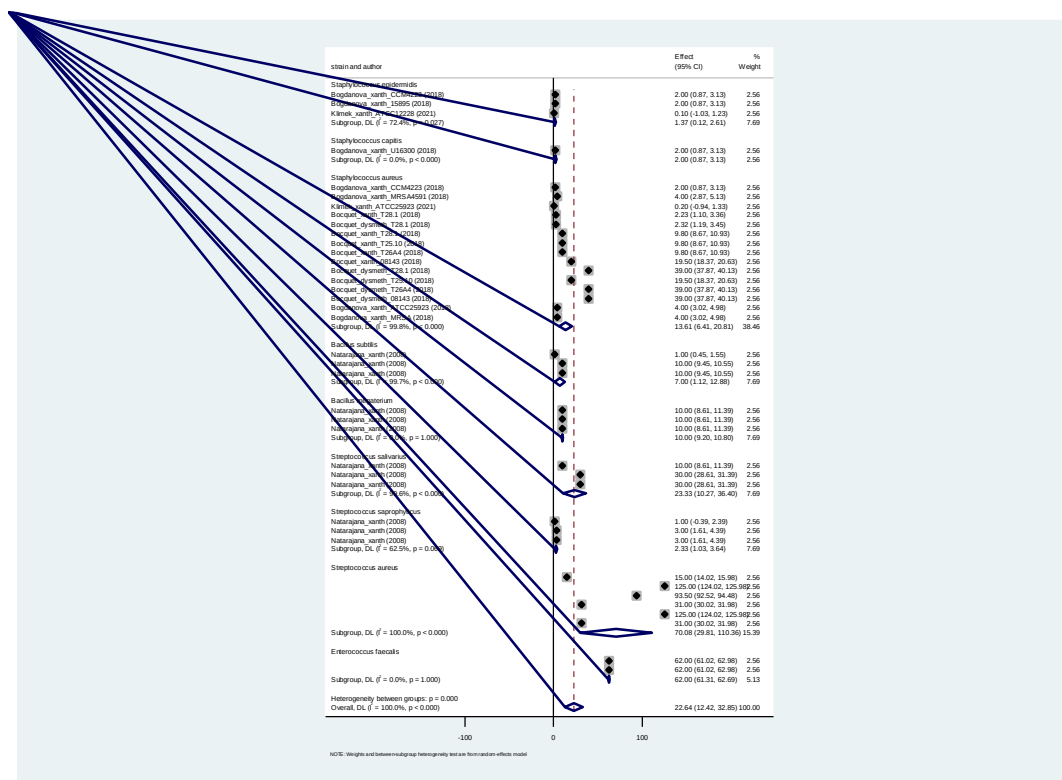


Figure 32: Forest plot showing flavonoids after 24h incubation against strains.

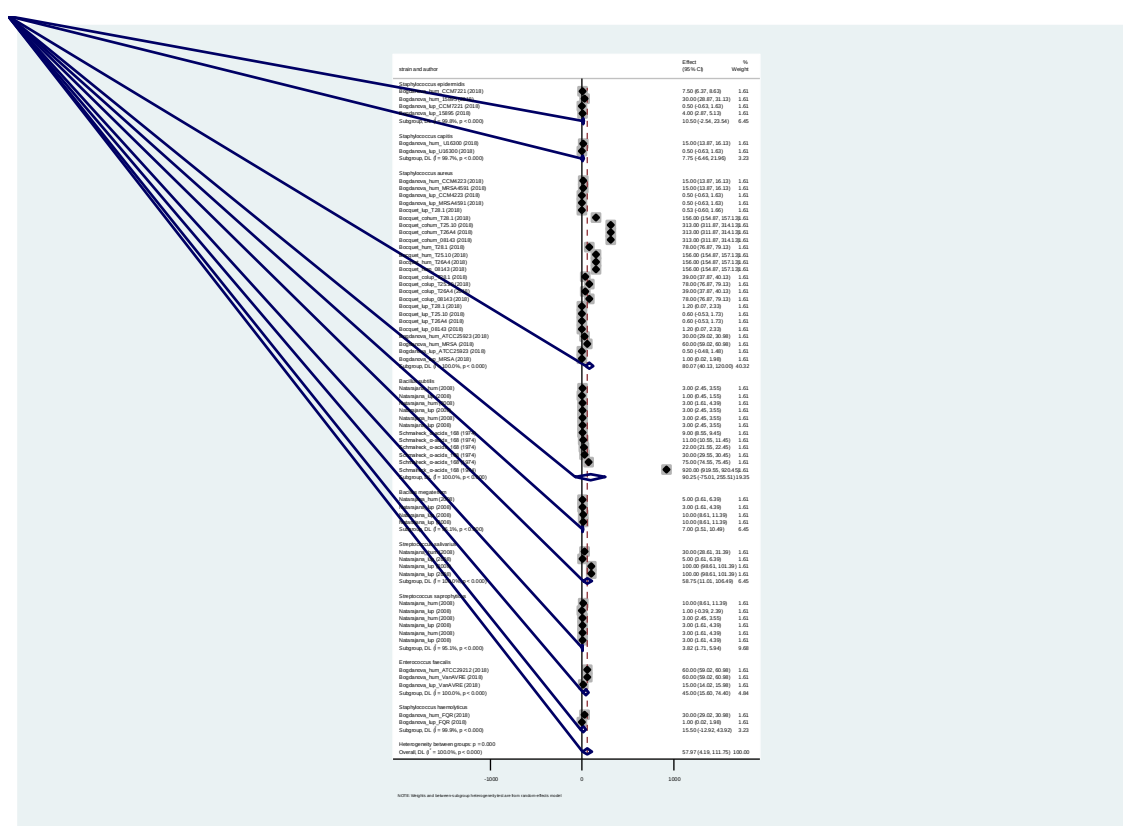


Figure 33: Forest plot showing bitter acids after 24h incubation against strains.

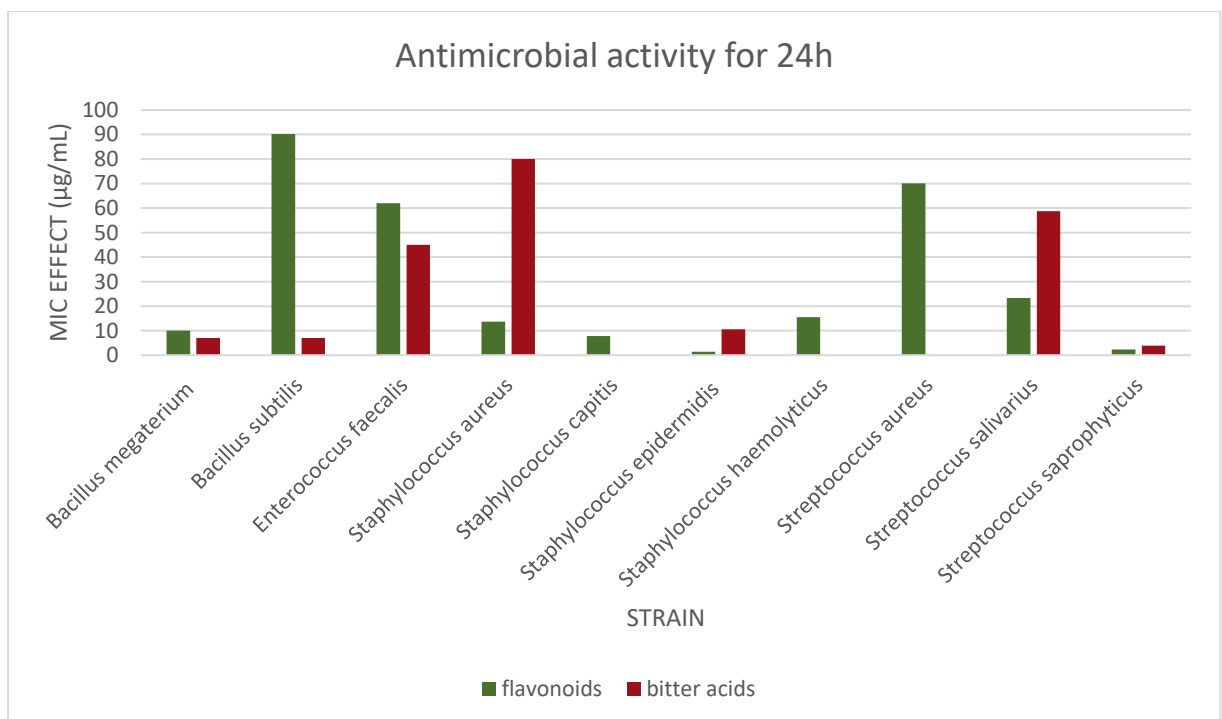


Figure 34: Minimum Inhibitory Concentration of meta-analysis of hop compounds' classes against microorganisms after 24h incubation. Green color stands for flavonoids and dark red for bitter acids.

Table 26: Results of meta-analysis process. The table illustrates MIC value along with Confidence Interval (CI), p-value after meta-analysis of classcompound3 against different strains for 48-hours incubation. Finally it shows the number of studies being used.

Hours	Number of studies	Strain	Classcompound3	MIC	CI (low - upper boundary)	p-value
48	3	Staphylococcus aureus	flavonoids	5,167	3,138-7,195	0
48	4	Listeria monocytogenes	flavonoids	129,675	(-)94,364-353,714	0
48	3	Escherichia coli	flavonoids	200	199,434-200,566	1
48	3	Salmonella enterica	flavonoids	200	199,434-200,566	1
48	7	Bacteroides fragilis	flavonoids	39,429	27,759-51,062	0
48	5	Clostridium perfringens	flavonoids	32,6	18,719-46,481	0
48	28	Clostridium difficile	flavonoids	59,036	51,644-66,428	0
48	2	Propionibacterium acnes	flavonoids	46,875	16,251-77,499	0
48	3	Bacillus subtilis	flavonoids	1200	569,96-1830,04	0
48	2	Pseudomonas fluorescens	flavonoids	1700	1699,2-1700,8	1
48	14	Bacteroides fragilis	bitter acids	512,857	287,914-737,8	0
48	10	Clostridium perfringens	bitter acids	630	323,008-936,992	0
48	56	Clostridium difficile	bitter acids	388	274,541-501,459	0
48	2	Candida albicans	bitter acids	375	130,005-619,995	0
48	2	Candida krusei	bitter acids	375	130,005-619,995	0
48	2	Candida parapsilosis	bitter acids	750	260,009-1239,991	0

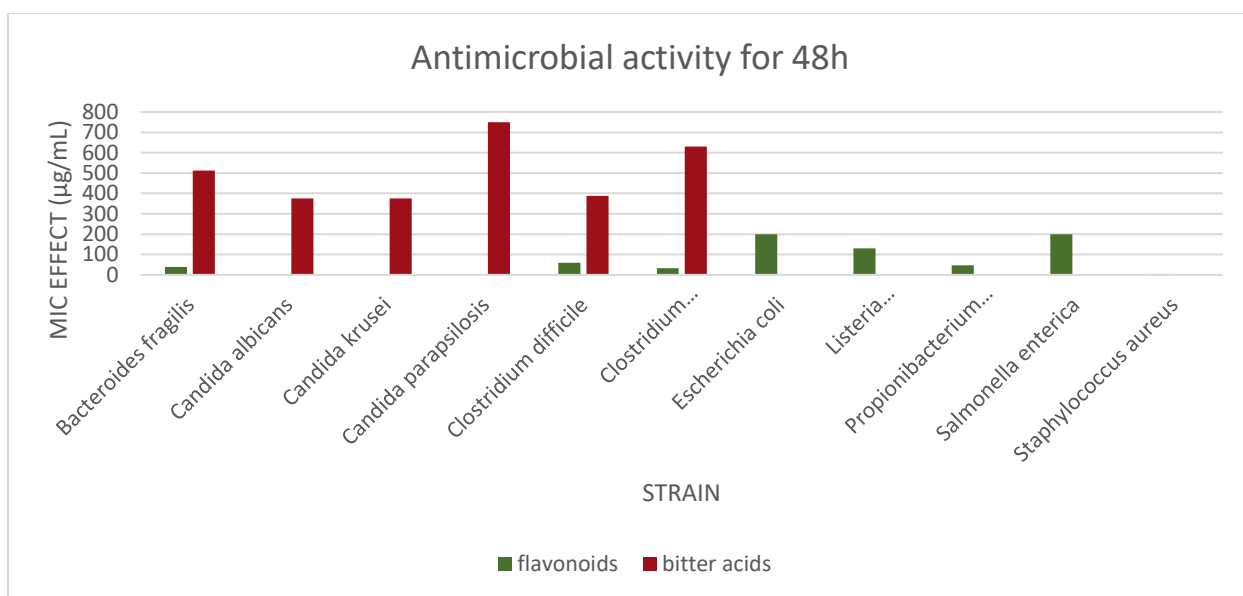


Figure 35: Minimum Inhibitory Concentration of meta-analysis of hop compounds' classes against microorganisms after 48h incubation. Green stands for flavonoids and dark red for bitter acids.

Table 27: Results of meta-analysis process. The table illustrates MIC value along with Confidence Interval (CI), p-value after meta-analysis of classcompound3 against different strains for 48-hours incubation. Finally, it shows the number of studies being used.

Hours	Number of studies	Strain	Classcompound3	MIC	CI (low - upper boundary)	p-value
24	4	Propionibacterium acnes	CO2-extract	3,49	2,728-4,247	0,144
24	6	Staphylococcus aureus	CO2-extract	6,32	2,205-10,425	0
24	2	Listeria monocytogenes	CO2-extract	10,00	9,307-10,693	1
24	2	Staphylococcus epidermidis	CO2-extract	0,10	(-)0,702-0,898	1
24	3	Streptococcus aureus	CO2-extract	1666,67	1013,345-2319,988	0
24	3	Enterococcus faecalis	CO2-extract	696,67	(-)580,689-1974,023	0
24	2	Enterococcus faecalis	hydralcoholic-extract	50,502	27,962-73,041	0
24	2	Staphylococcus aureus	hydralcoholic-extract	39	38,2-39,8	1
24	2	Staphylococcus epidermidis	hydralcoholic-extract	68,5	10,681-126,319	0
24	2	Staphylococcus lugdunensis	hydralcoholic-extract	390,5	(-)69,112-850,112	0

24	2	Staphylococcus warneri	hydralcoholic-extract	332	(-)242,269-906,269	0
24	2	Streptococcus agalactiae	hydralcoholic-extract	58,5	20,281-96,179	0
24	2	Pseudomonas aeruginosa	hydralcoholic-extract	625	624,2-625,8	1
24	3	Candida albicans	hydralcoholic-extract	273,333	(-)77,594-624,261	0
24	3	Streptococcus aureus	hydralcoholic-extract	62,333	0,921-123,746	0
24	14	Staphylococcus aureus	hydroacetic-extract	55,657	12,151-99,163	0

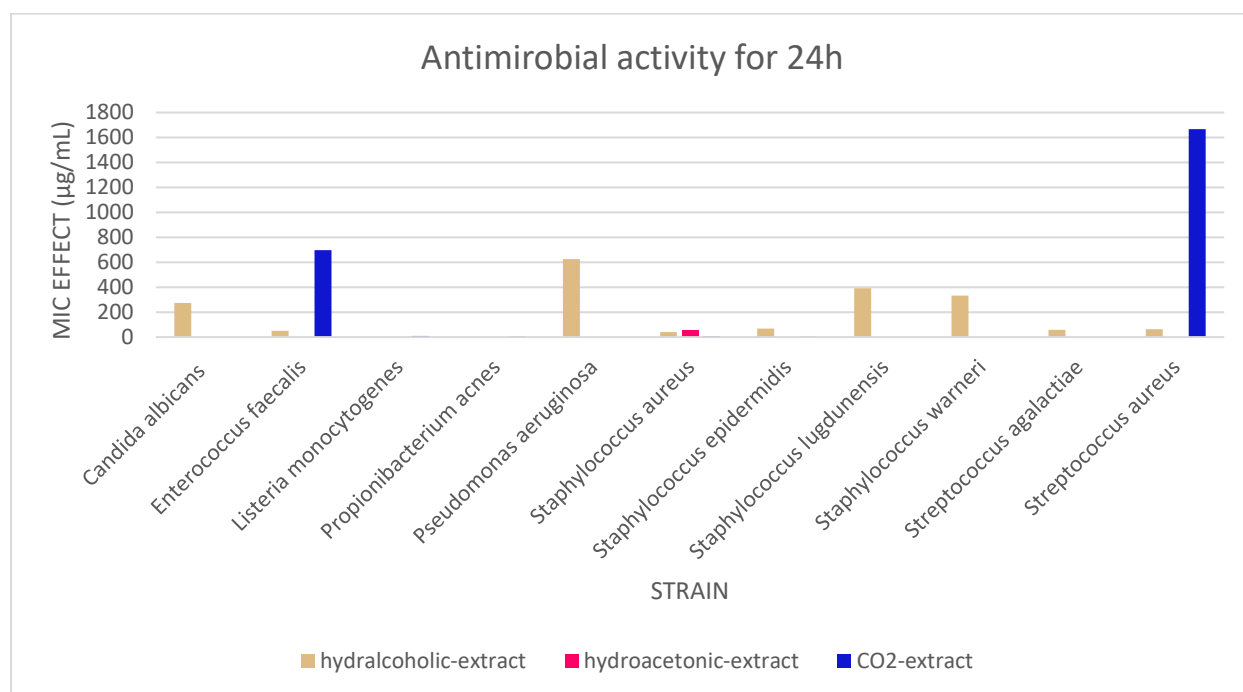


Figure 36: Minimum Inhibitory Concentration of meta-analysis of hop extracts against miroorganisms after 24h incubation. Beige stands for hydralcoholic-extract, pink for hydroacetic-extract and blue for CO2-extract.

Table 28: Results of meta-analysis process. The table illustrates MIC value along with Confidence Interval (CI), p-value after meta-analysis of classcompound3 against different strains for 48-hours incubation. Finally, it shows the number of studies being used.

Hours	Number of studies	Strain	Classcompound3	MIC	CI (low - upper boundary)	p-value
48	7	Staphylococcus aureus	CO2-extract	46,43	(-)6,222-99,080	0
48	7	Listeria monocytogenes	CO2-extract	37,19	(-)16,563-90,934	0
48	6	Escherichia coli	CO2-extract	2604,17	1041,287-4167,047	0
48	6	Salmonella enterica	CO2-extract	2604,17	1041,287-4167,047	0
48	2	Streptococcus mutans	CO2-extract	0,39	(-)0,409-1,191	1
48	2	Streptococcus sanguinis	CO2-extract	0,78	(-)0,019-1,581	1
48	4	Propionibacterium acnes	CO2-extract	15,63	15,059-16,191	1
48	6	Bifidobacteriumm dentium	hydralcoholic-extract	213,333	160,444-266,223	0
48	6	Bifidobacterium longum	hydralcoholic-extract	96	67,951-124,049	0
48	6	Lactobacillus salivarius	hydralcoholic-extract	138,667	88,318-189,016	0
48	6	Streptococcus mutans	hydralcoholic-extract	106,667	80,222-133,111	0
48	6	Streptococcus salivarius	hydralcoholic-extract	34,667	22,079-47,254	0
48	6	Streptococcus sobrinus	hydralcoholic-extract	66,667	38,135-95,198	0
48	12	Fusobacterium nucleatum	hydralcoholic-extract	250,667	154,914-346,419	0
48	4	Candida albicans	hydralcoholic-extract	384	239,157-528,843	0
48	14	Lactobacillus acidophilus	hydroacetic-extract	92,257	71,858-112,656	0

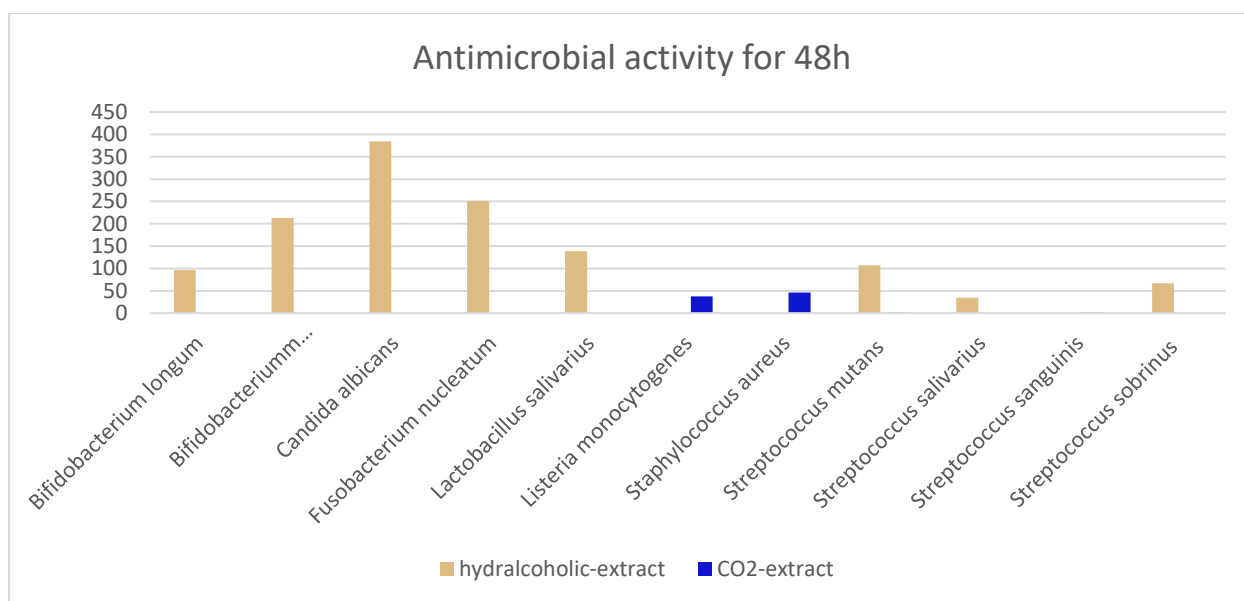


Figure 37: Minimum Inhibitory Concentration of meta-analysis of hop extracts against microorganisms after 48h incubation. Beige stands for hydralcoholic-extract and blue for CO2-extract.

In those diagrams, both in 24h and in 48h incubation flavonoids generally have better antimicrobial activity than bitter acids. In the first conditions, *Staphylococcus aureus* with MIC value 13,609 µg/mL, *Staphylococcus epidermidis* with 1,366 µg/mL, *Streptococcus salivarius* with 23,333 µg/mL and *Streptococcus saprophyticus* with 2,333 µg/mL have better values than the corresponding of bitter acids, while in the second conditions *Bacteroides fragilis* with 39,429 µg/mL, *Clostridium difficile* with 59,036 µg/mL and *Clostridium perfringens* with 32,6 µg/mL, flavonoids have also better activity than bitter acids.

We performed metabias analysis as well and the results showed that there was not any bias in our studies, because the bias value was higher than 0.05.

3.3.3.2 By phylum

The diagrams here illustrate the meta-analysis of classcompound3 against the stratification of microorganisms in Phylum.

Table 29: Results of meta-analysis process. The table illustrates MIC value along with Confidence Interval (CI), p-value after meta-analysis of classcompound3 against different strains in Phylum stratification for 24-hours incubation. Finally, it shows the number of studies being used.

Hours	Number of studies	Phylum	Classcompound3	MIC	CI (low - upper boundary)	p-value
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24	39	Bacillota	flavonoids	22,635	12,419-32,825	0
24	62	Bacillota	bitter acids	57,97	4,187-111,572	0

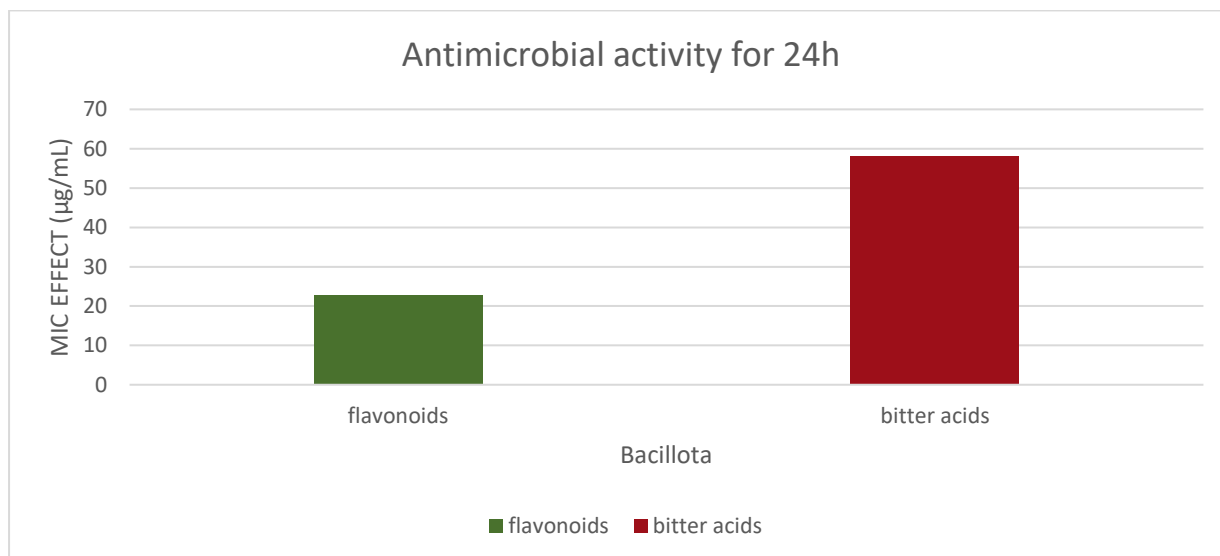


Figure 38: Minimum Inhibitory Concentration of meta-analysis of hop compounds' classes against microorganisms after 24h incubation. Green stands for flavonoids and dark red for bitter acids.

Table 30: Results of meta-analysis process. The table illustrates MIC value along with Confidence Interval (CI), p-value after meta-analysis of classcompound3 against different strains in Phylum stratification for 24-hours incubation. Finally, it shows the number of studies being used.

Hours	Number of studies	Phylum	Classcompound3	MIC	CI (low - upper boundary)	p-value
24	4	Actinomycetota	CO2-extract	3,488	2,728-4,247	0,144
24	19	Bacillota	CO2-extract	377,531	58,671-696,391	0
24	2	Actinomycetota	hydralcoholic-extract	39	38,2-39,8	1
24	17	Bacillota	hydralcoholic-extract	132,941	45,341-220,542	0
24	4	Pseudomonadota	hydralcoholic-extract	625	624,434-625,566	1
24	3	Ascomycota	hydralcoholic-extract	273,333	(-)-77,594-624,261	0
24	14	Bacillota	hydroacetonc-extract	55,657	12,151-99,163	0

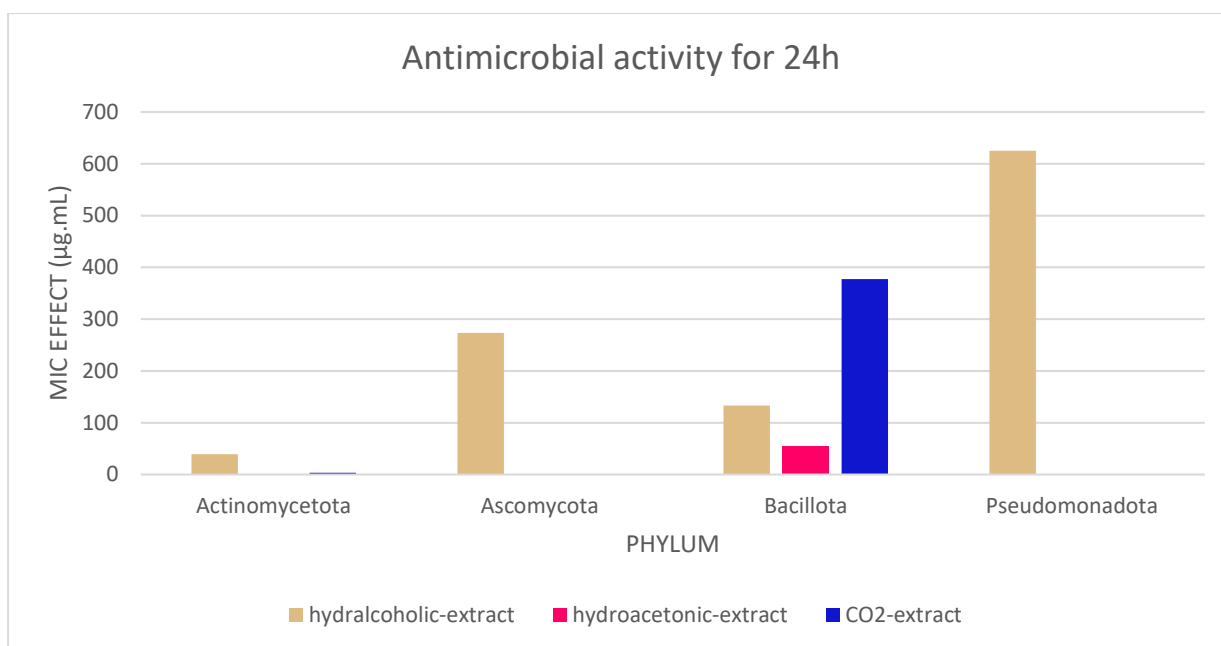


Figure 39: Minimum Inhibitory Concentration of meta-analysis of hop extracts against microorganisms after 24h incubation. Beige for hydralcoholic-extract, pink for hydroacetonc-extract and blue for CO2-extract.

Table 31: Results of meta-analysis process. The table illustrates MIC value along with Confidence Interval (CI), p-value after meta-analysis of classcompound3 against different strains in Phylum stratification for 48-hours incubation. Finally it shows the number of studies being used.

Hours	Number of studies	Phlum	Classcompound3	MIC	CI (low - upper boundary)	p-value
48	52	Bacillota	flavonoids	193,834	40,886-346,782	0
48	8	Pseudomonadota	flavonoids	575	130,098-1019,902	0
48	7	Bacteroida	flavonoids	39,429	27,795-51,062	0
48	2	Actinomycetota	flavonoids	46,875	16,251-77,499	0
48	4	Ascomycota	flavonoids	462,5	(-)286,149-1211,149	0
48	14	Bacteroida	bitter acids	512,857	287,914-737,8	0
48	66	Bacillota	bitter acids	424,667	316,665-532,668	0
48	7	Ascomycota	bitter acids	571,429	339,269-803,588	0

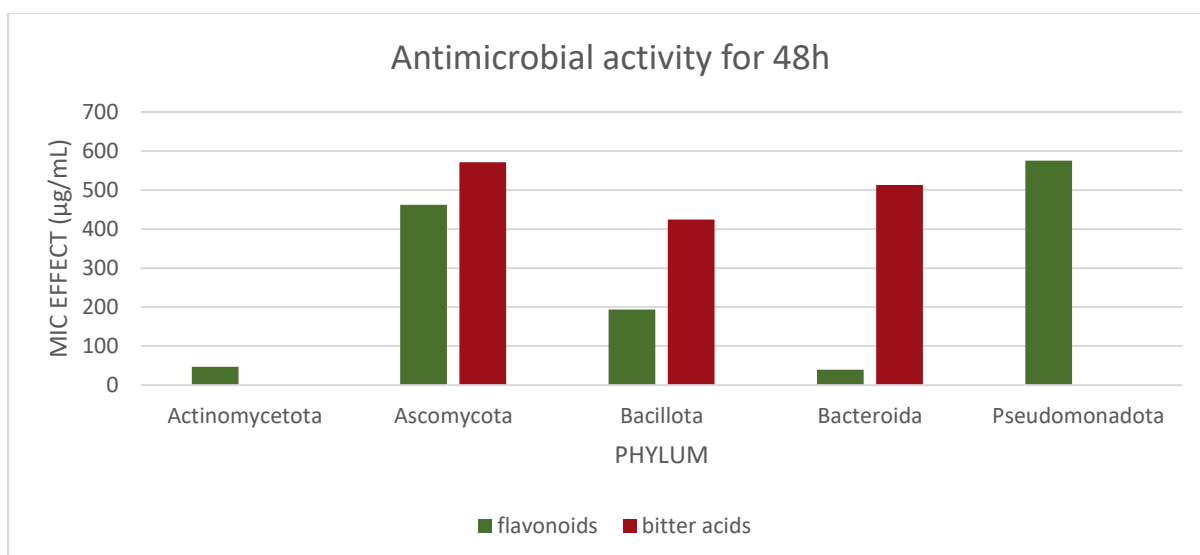


Figure 40: Minimum Inhibitory Concentration of meta-analysis of hop compounds' classes against microorganisms after 48h incubation. Green stands for flavonoids and dark red for bitter acids.

Table 32: Results of meta-analysis process. The table illustrates MIC value along with Confidence Interval (CI), p-value after meta-analysis of classcompound3 against different strains in Phylum stratification for 48-hours incubation. Finally, it shows the number of studies being used.

Hours	Number of studies	Phlum	Classcompound3	MIC	CI (low - upper boundary)	p-value
48	19	Bacillota	CO2-extract	32,163	7,247-57,979	0
48	12	Pseudomonadota	CO2-extract	2604,167	1550,473-3657,86	0
48	4	Actinomycetota	CO2-extract	15,625	15,059-16,191	1
48	4	Ascomycota	CO2-extract	500	153,524-846,476	0
48	12	Actinomycetota	hydralcoholic-extract	154,667	109,761-199,572	0
48	24	Bacillota	hydralcoholic-extract	86,667	64,579-108,754	0
48	12	Fusobacteriota	hydralcoholic-extract	250,667	154,914-346,419	0
48	4	Ascomycota	hydralcoholic-extract	384	239,157-528,843	0
48	14	Bacillota	hydroacetic-extract	92,257	71,858-112,656	0

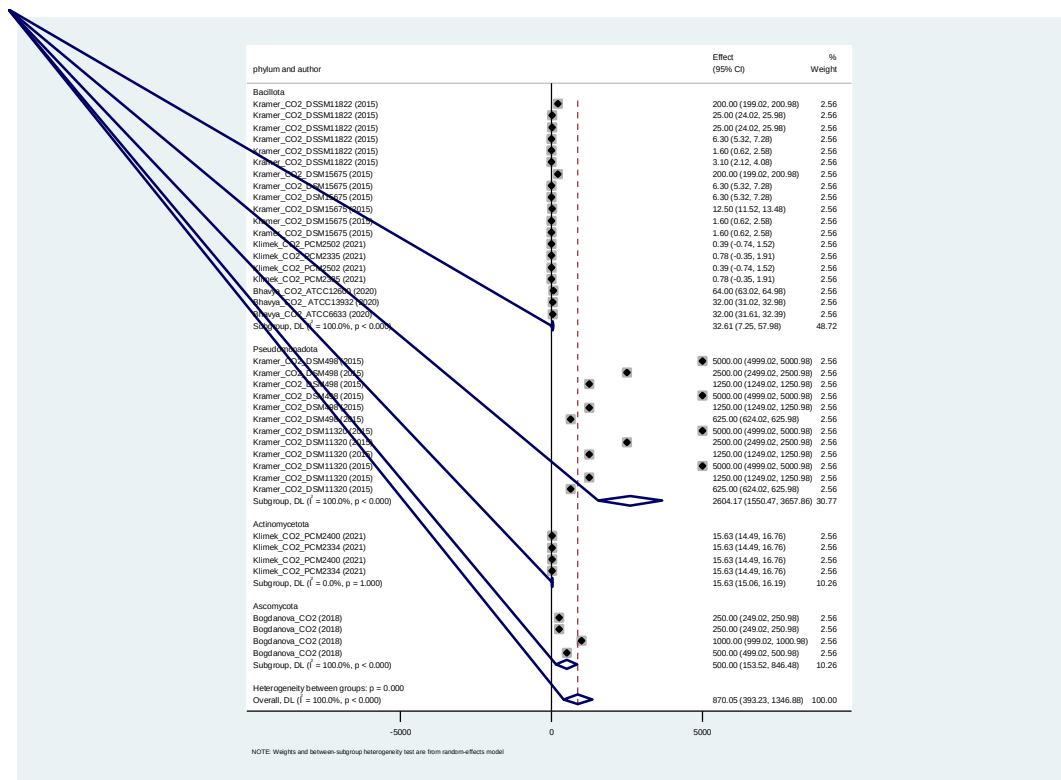


Figure 41: Forest plot showing the CO₂-extract after 48h incubation against Phylum.

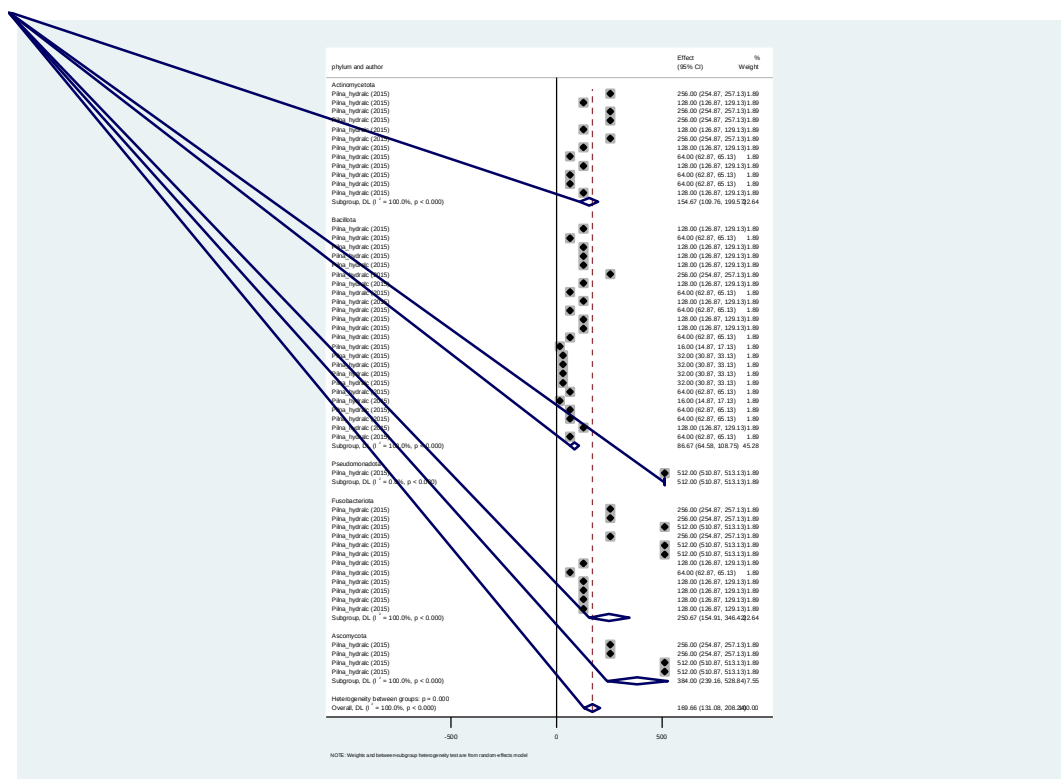


Figure 42: Forest plot showing the hydralcoholic-extract after 48h incubation against Phylum.

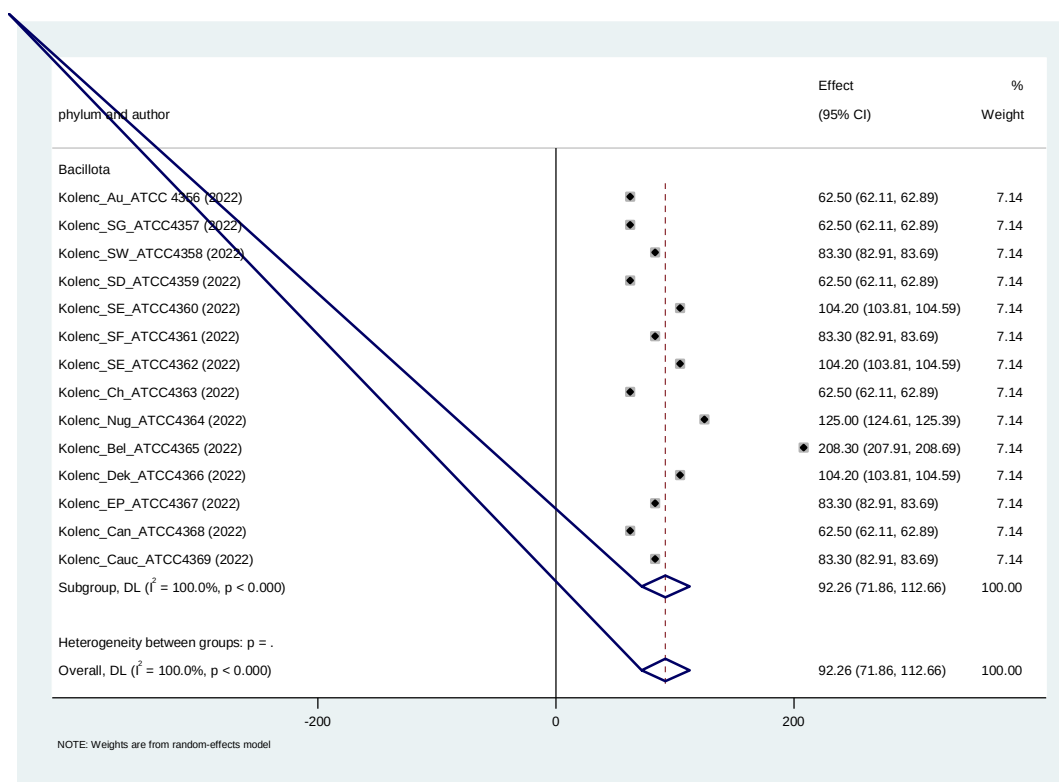


Figure 43: Forest plot showing hydroacetic-extract after 48h incubation against Phylum.

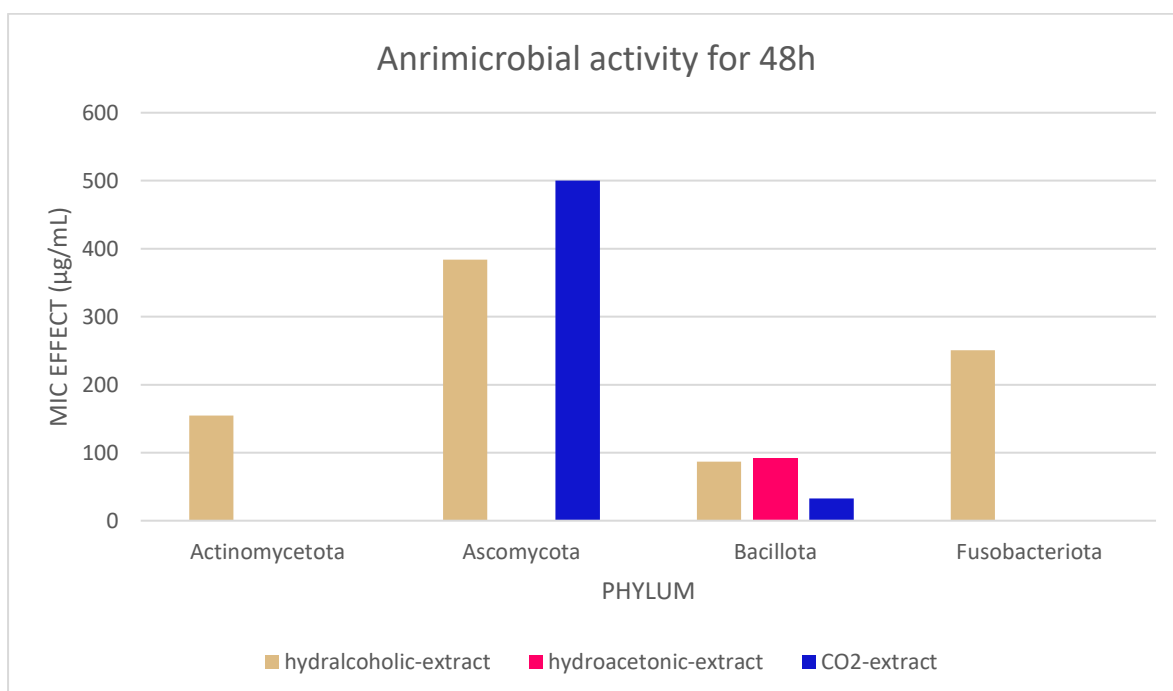


Figure 44: Minimum Inhibitory Concentration of meta-analysis of hop extracts against microorganisms after 48h incubation. Beige stands for hydralcoholic-extract, blue for CO2-extract and pink for hydroacetic-extract

Finally, both in 24 hours and 48 hours incubation flavonoids have better activity against Bacillota with MIC value 22,635 µg/mL in contrast to bitter acids with value 57,97 µg/mL in 24h and 193,834 µg/mL, 424,667 µg/mL respectively in 48h. Moreover, totally flavonoids in 48h incubation have stronger antimicrobial activity, as we can see against Ascomycota (MIC flavonoids: 462,5 µg/mL, MIC bitter acids: 571,429 µg/mL) and Bacteroida (MIC flavonoids: 39,429 µg/mL, MIC bitter acids: 512,857 µg/mL).

In 24h incubation hydroacetic-extract against Bacillota has MIC 55,657µg/mL, hydralcoholic-extract 132,941 µg/mL and CO2-extract 377,531 µg/mL. Therefore hydroacetic-extract has the best activity, a fact that is been reversed in 48h because hydroacetic-extract has the weakest activity with MIC value being 92,257 µg/mL, hydralcoholic-extract 86,667 µg/mL and CO2-extract 32,613 µg/mL.

The other phylum classes have not enough data to compare them.

After the metabias, we observed that there is not any bias in our meta-analysis study, because the value was higher than 0,05.

3.3.3.3 By probiotic, food spoilage, pathogenicity

The diagrams here illustrate the meta-analysis of classcompound2 against the stratification of microorganisms into probiotic, pathogenic and food spoilage activity.

Table 33: Results of meta-analysis process. The table illustrates MIC value along with Confidence Interval (CI), p-value after meta-analysis of classcompound2 against stratification of microorganisms in probiotic, pathogenic and food-spoilage for 24-hours incubation. Finally it shows the number of studies being used.

Hours	Number of studies	probiotic/ food spoilage/ pathogenic	Classcompound3	MIC	CI (low - upper boundary)	p-value
24	33	food spoilage	flavonoids	22,808	11,54-34,077	0
24	51	food spoilage	bitter acids	66,091	3,228-128,594	0
24	39	opportunistic pathogens	flavonoids	22,635	12,419-32,852	0
24	62	opportunistic pathogens	bitter acids	57,97	4,187-111,752	0
24	6	probiotic	flavonoids	8,468	4,701-12,27	0
24	16	probiotic	bitter acids	69,438	(-)70,429-209,314	0
24	12	food spoilage	CO2-extract	421,908	0,947-842,868	0
24	9	food spoilage	hydralcoholic-extract	53,667	32,422-74,912	0

24	14	food spoilage	hydroacetic- extract	55,657	12,151- 99,163	0
24	23	opportunistic pathogens	CO2-extract	355,741	75,21- 636,272	0
24	25	opportunistic pathogens	hydralcoholic- extract	220,08	119,665- 320,495	0
24	14	opportunistic pathogens	hydroacetic- extract	55,657	12,151- 99,163	0
24	2	probiotic	CO2-extract	502,5	(-)-472,582- 1477,582	0

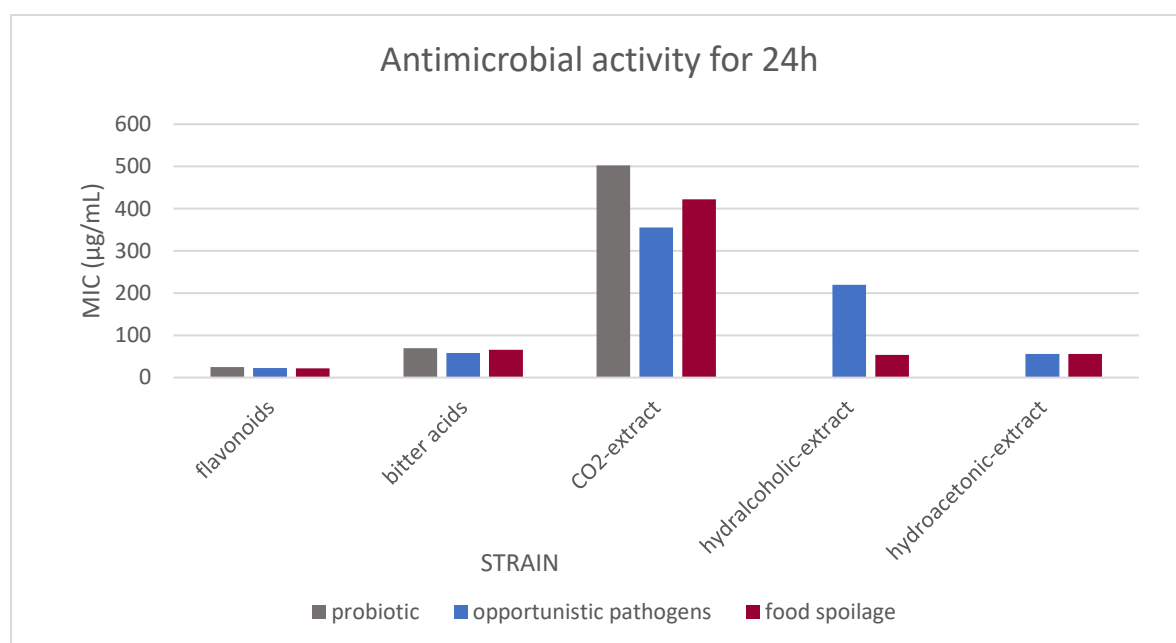


Figure 45: Minimum Inhibitory Concentration of meta-analysis of hop compounds and extracts after 24h incubation against different microorganisms after stratification in probiotic, pathogenic, food-spoilage. Grey stands for probiotic, blue for opportunistic pathogens, baby blue for pathogens and red for food spoilage.

Table 34: Results of meta-analysis process. The table illustrates MIC value along with Confidence Interval (CI), p-value after meta-analysis of classcompound2 against stratification of microorganisms in probiotic, pathogenic and food-spoilage for 48-hours incubation. Finally, it shows the number of studies being used.

Hours	Number of studies	probiotic/ food spoilage/ pathogenic	Classcompound3	MIC	CI (low - upper boundary)	p-value
48	26	food spoilage	flavonoids	242,245	9,612- 474,879	0

48	11	food spoilage	bitter acids	573,636	277,535-869,738	0
48	6	pathogenic	flavonoids	215	(-)9,964-439,965	0
48	3	pathogenic	bitter acids	583,333	151,202-1015,465	0
48	69	opportunistic pathogens	flavonoids	259,552	122,97-396,135	0
48	85	opportunistic pathogens	bitter acids	440,8	347,855-533,745	0
48	13	probiotic	flavonoids	459,692	85,838-833,547	0
48	14	probiotic	bitter acids	512,857	287,914-737,8	0
48	31	food spoilage	CO2-extract	1028,053	448,059-1608,047	0
48	24	food spoilage	hydralcoholic-extract	86,667	64,579-108,754	0
48	14	food spoilage	hydroacetic-extract	92,257	71,858-112,656	0
48	8	pathogenic	CO2-extract	2109,375	793,746-3425,004	0
48	31	opportunistic pathogens	CO2-extract	550,23	105,87-994,591	0
48	53	opportunistic pathogens	hydralcoholic-extract	169,66	131,083-208,238	0
48	14	opportunistic pathogens	hydroacetic-extract	92,257	71,858-112,656	0
48	18	probiotic	hydralcoholic-extract	149,333	115,699-182,967	0
48	14	probiotic	hydroacetic-extract	92,257	71,858-112,656	0

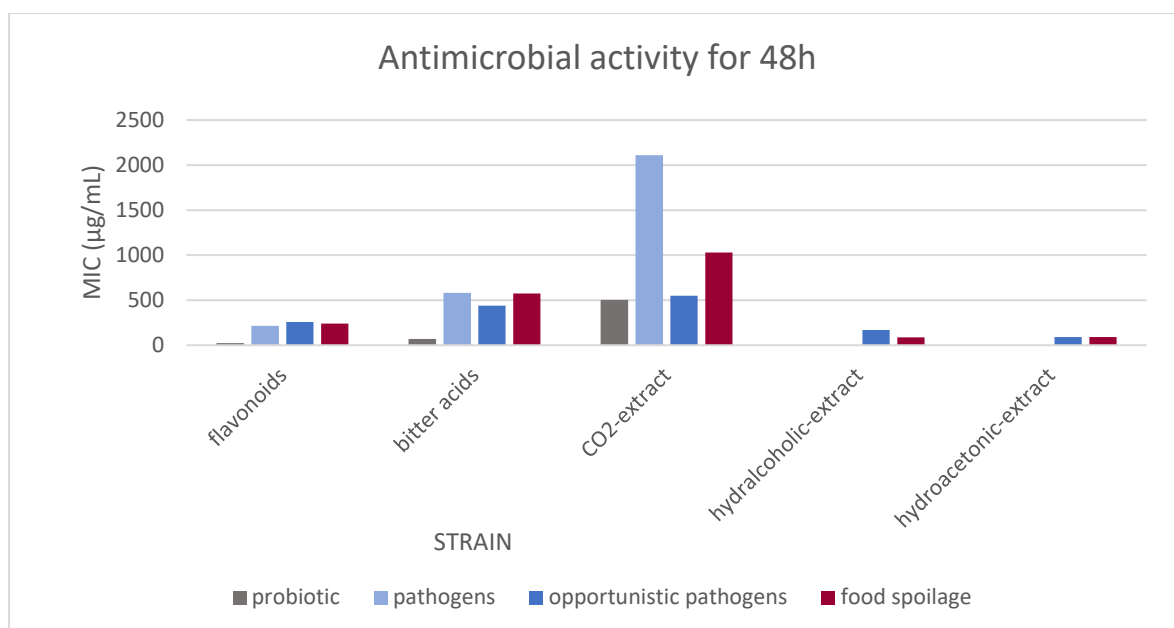


Figure 46: Minimum Inhibitory Concentration of meta-analysis of hop compounds and extracts after 48h incubation against different microorganisms after stratification in probiotic, pathogenic, food-spoilage. Grey stands for probiotic, blue for opportunistic pathogens, baby blue for pathogens and red for food spoilage.

In those diagrams, we observe that flavonoids have the best activity in all three categories.

To be more specific in 24h incubation, referring to probiotic, flavonoids with MIC value 25,20 µg/mL seems to be more strong than bitter acids and CO2-extract (MIC: 69,44 µg/mL, 502,5 µg/mL), whereas hydralcoholic and hydroacetic-extract have no data. Furthermore, flavonoids against opportunistic pathogens have also stronger antimicrobial activity with MIC value equal to 22,64 µg/mL, being followed by bitter acids with MIC 57,97 µg/mL, while among extracts hydralcoholic has the best one with MIC value equal to 220 µg/mL.

In 48h incubation, although flavonoids have in pathogens, opportunistic pathogens, food spoilage stronger antimicrobial activity (MIC: 215 µg/mL, 259,6 µg/mL, 242,2 µg/mL respectively) than bitter acids (MIC: 583,3 µg/mL, 440,8 µg/mL, 573,6 µg/mL respectively), in probiotics bitter acids (MIC: 69,4 µg/mL) seems to have better one than flavonoids (MIC 459,7 µg/mL).

We performed metabias and as a result we found that bias value is higher than 0.05.

4 Discussion

Humulus lupulus is a dioecious climbing plant belonging to the family of the Cannabinaceae and it is used mainly in brewing factory in order to maintain and enhance the flavor of the beer. It is commonly used because of its aroma and taste of bitterness in beer as well as its contribution to human health. Hops seems to have many significant benefits, like anticancer, anti-inflammatory, antioxidant, sedative and estrogenic activity as well as antimicrobial activity, which is the main subject of this meta-analysis study.

In this meta-analysis process, we tried to find out the antimicrobial activity of hop's compounds and extracts, by calculating the MIC value. We resulted in 18 articles, from which we ended up having 450 reports, where we found 6 hop compounds, 3 hop extracts and 55 different microorganisms.

Before the meta-analysis process, we divided the compounds and extracts into three classes and we investigated the antimicrobial activity in both 24 and 48h incubation. In the first compound classification we found out that xanthohumol has the best antimicrobial activity among compounds, except for the occasion of *Bacillus megaterium* and *subtilis*, where lupulone has the best one. Simultaneously, among extracts, hydralcoholic-extract has the best antimicrobial activity in both 24 and 48h incubation although only in the *Staphylococcus aureus* microorganisms, CO₂-extract has the best activity.

In the classification compound 3, flavonoids seem to have better activity against most of the microorganisms than bitter acids in 24h incubation, and in 48h incubation flavonoids have better activity than bitter acids, which seems to have higher MIC values than in 24h due to the existence of different microorganisms.

Another stratification that we made included division of microorganisms in whether they are pathogenic for humans for beneficial. That's why we divided them in probiotic, pathogenic and food spoilage microorganisms. We found out that lupulone from hop compounds in 24h incubation has the best antimicrobial activity in all three categories, and hydroacetic extract has the best one in probiotic and opportunistic pathogens and hydralcoholic in the food spoilage category against microorganisms. In 48h incubation xanthohumol seems to have the best activity among other compounds, and when referring to extracts the results are the same. Furthermore, in compound classification 3, flavonoids are the ones having the best MIC values in 24h, although in 48h we observed better activity of bitter acids against probiotic, which is a result of existence of different microorganisms.

In conclusion, we observed that both flavonoids and bitter acids have the same antimicrobial activity against probiotic microorganisms as well as against pathogenic and food spoilage. Same condition seems to be confirmed in hop extracts too.

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6 Appendix

6.1 Metabias data

More metabias data are available in this section, by showing forest plots as a result of STATA13.1.

6.1.1 Metabias in Compound classification 3

The forest plot refers to bitter acids in 24h incubation, where the bias value is 0.206, higher than 0.05, thus we have no bias in this study selection.

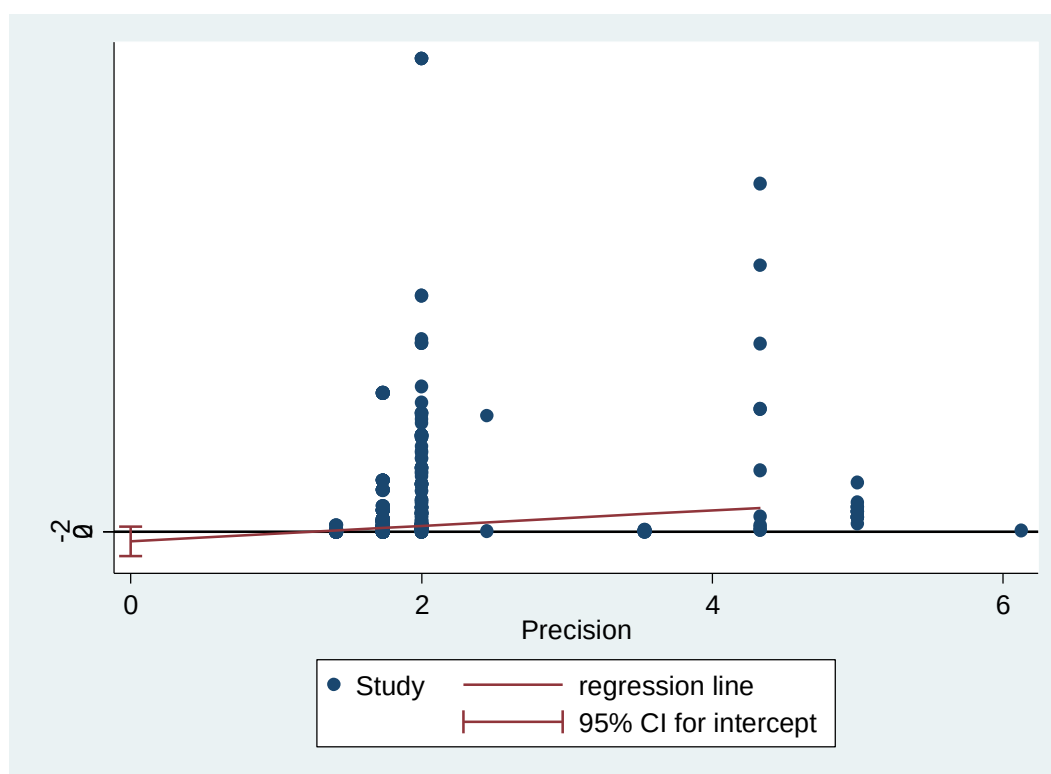


Figure 47: Metabias forest plot for bitter acids in 24h incubation.

The forest plot refers to bitter acids in 48h incubation, where the bias value is 0.476, higher than 0.05, thus we have no bias in this study selection

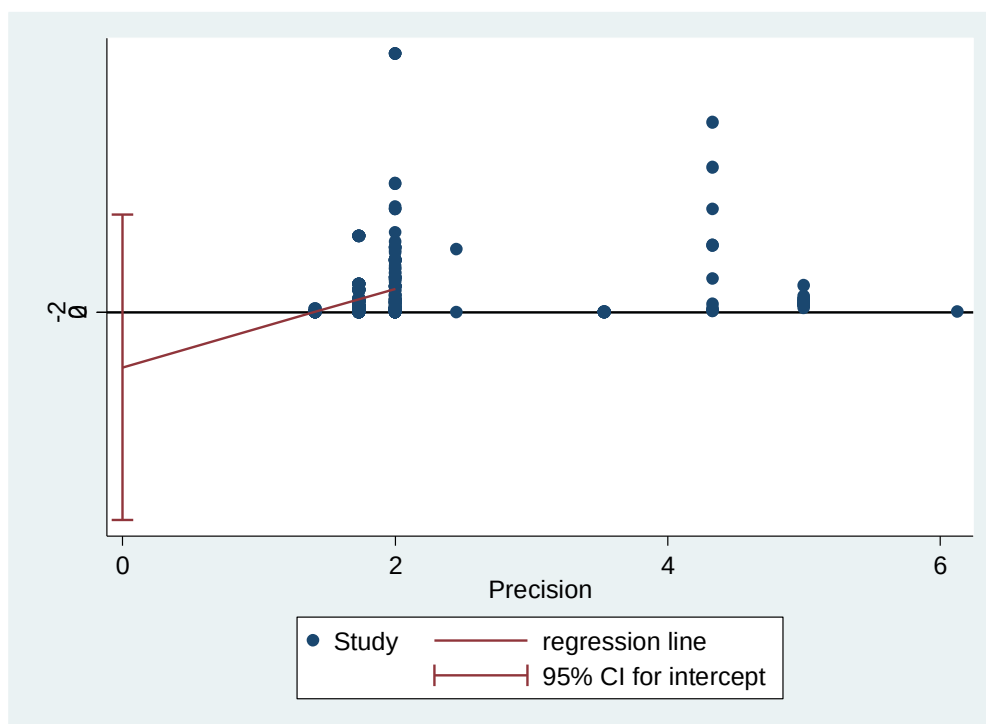


Figure 48: Metabias forest plot for bitter acids in 48h incubation.

The forest plot here presents flavonoids in 24h incubation, where the bias value is 0,677, higher than 0.05, thus we have no bias in this study selection.

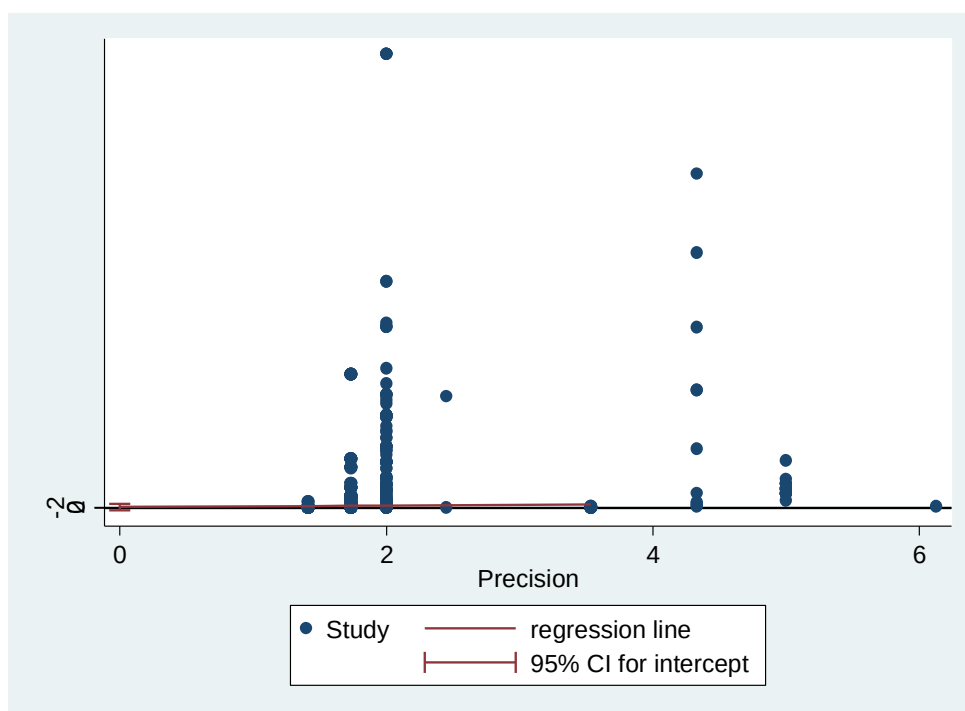


Figure 49: Metabias forest plot for flavonoids in 24h.

The forest plot here presents flavonoids in 48h incubation, where the bias value is 0.000, meaning that there is bias in this study selection.

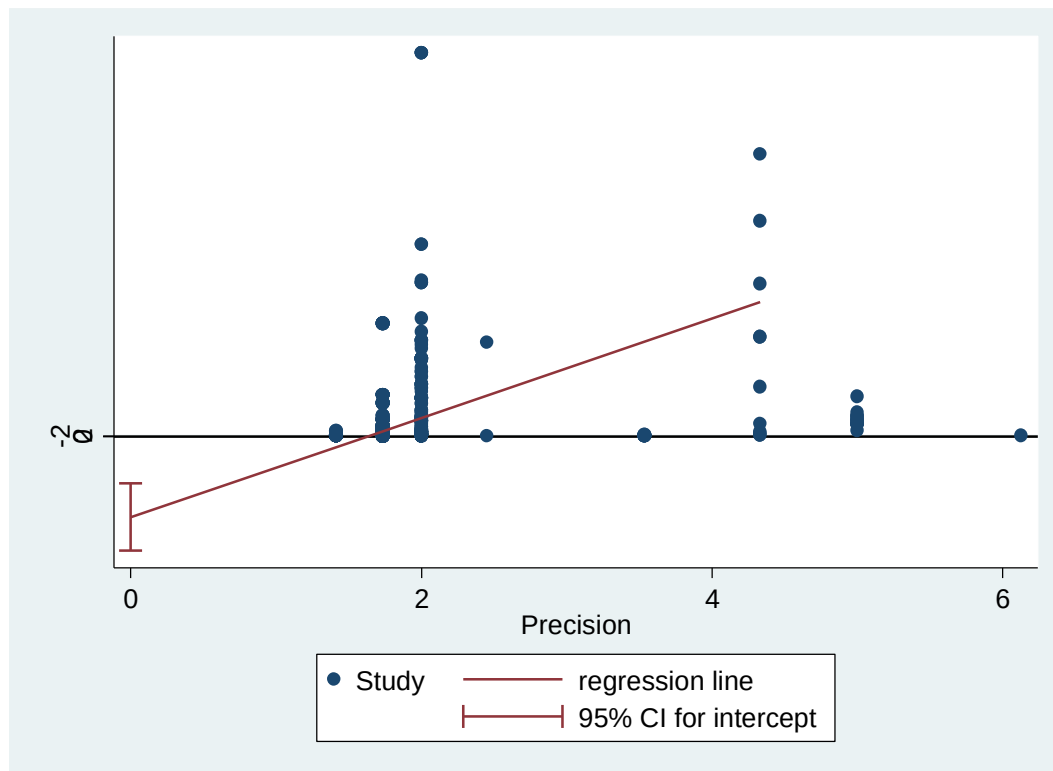


Figure 50: Metabias forest plot for flavonoids in 48h incubation.

The forest plot presents CO₂-extract in 24h incubation, where the bias value is 0.365, higher than 0.05, thus we have no bias in this study selection.

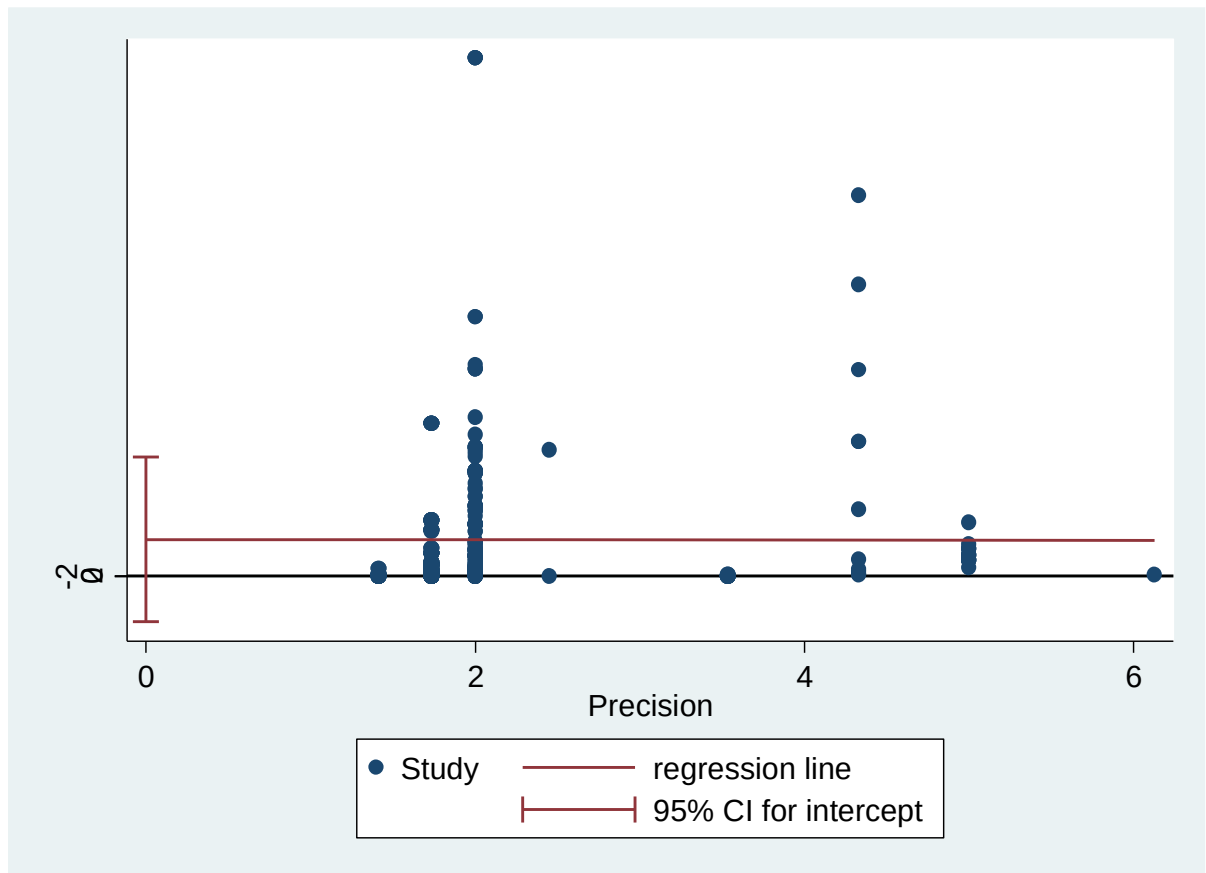


Figure 51: Metabias forest plot for CO₂-extract in 24h incubation

The following forest plot illustrates the CO₂-extract in 48h incubation, where bias value is 0.360, higher than 0.05, thus we have no bias in this study selection.

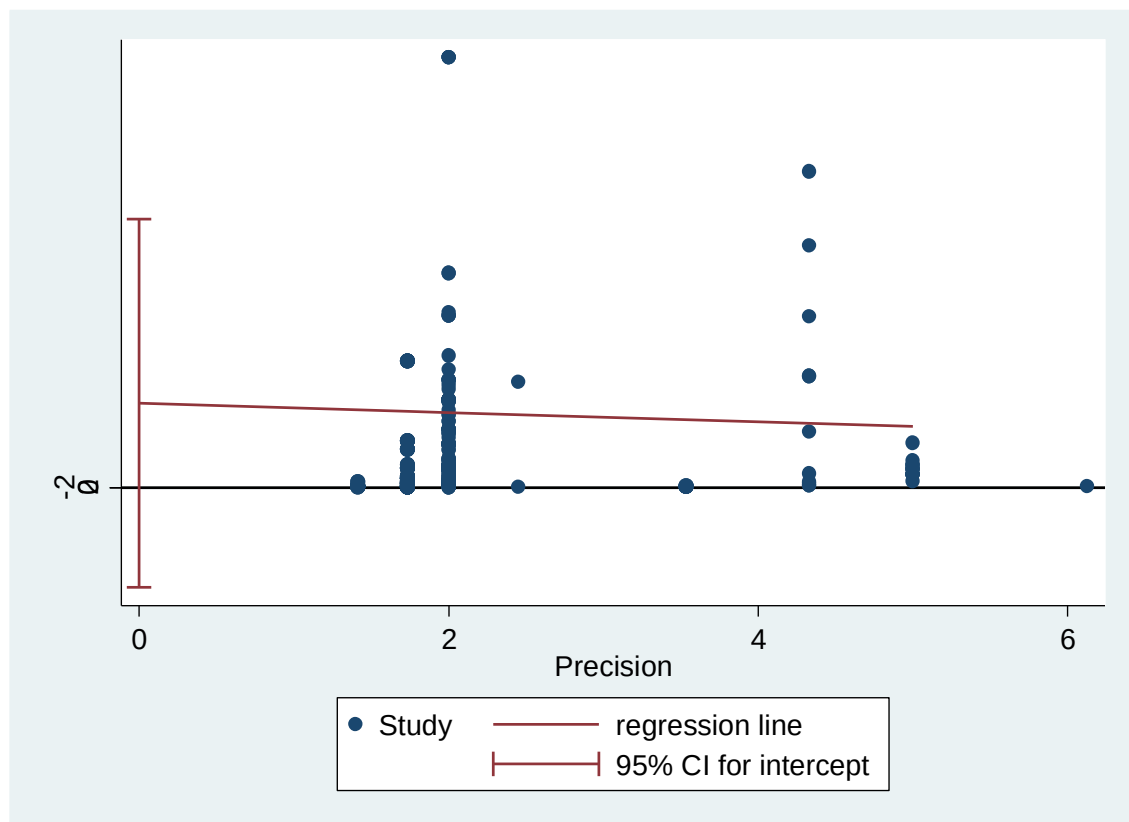


Figure 52: Metabias forest plot for CO₂-extract in 48h incubation.

The following forest plot illustrates the hydralcoholic-extract in 24h incubation, where bias value is 0.143 higher than 0.05, thus we have no bias in this study selection.

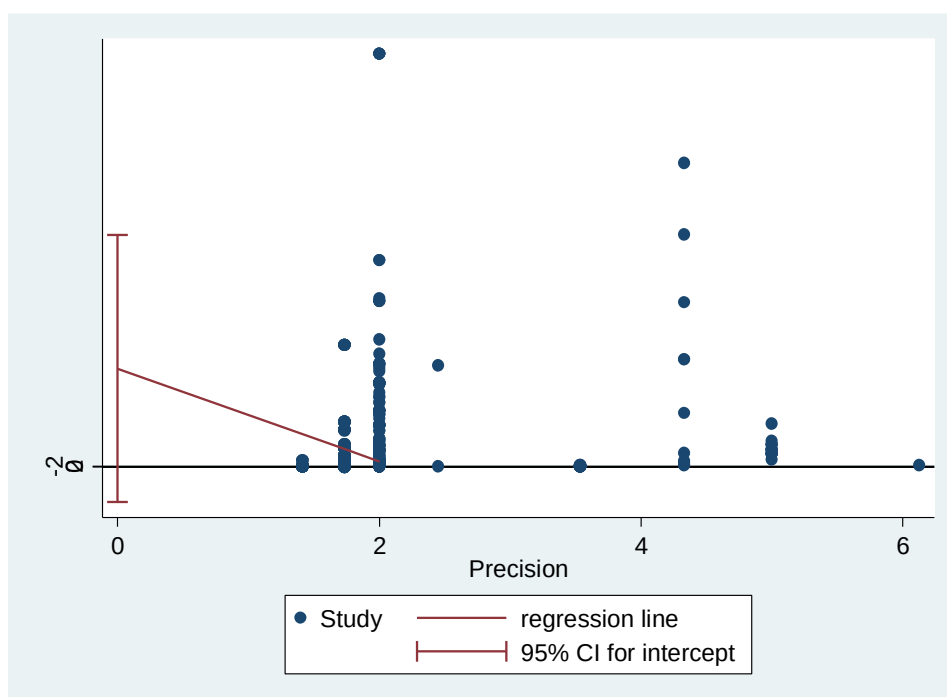


Figure 53: Metabias forest plot for hydralcoholic-extract in 24h incubation

The forest plot illustrates the hydralcoholic-extract in 48h incubation, where bias value is 0.000 less than 0.05, meaning that it has statistic bias.

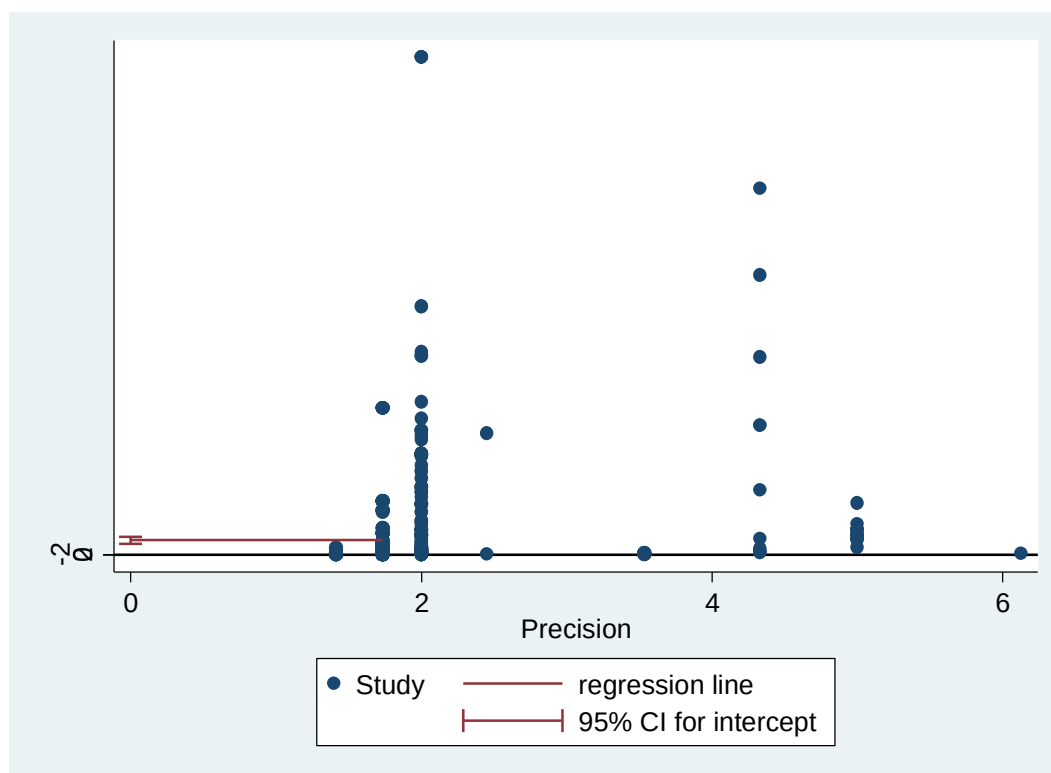


Figure 54: Metabias forest plot showing hydralcoholic-extract in 48h incubation.

The following forest plot illustrates the hydroacetonic-extract in 24h incubation, where bias value is 0.026 higher than 0.05, thus we have no bias in this study selection.

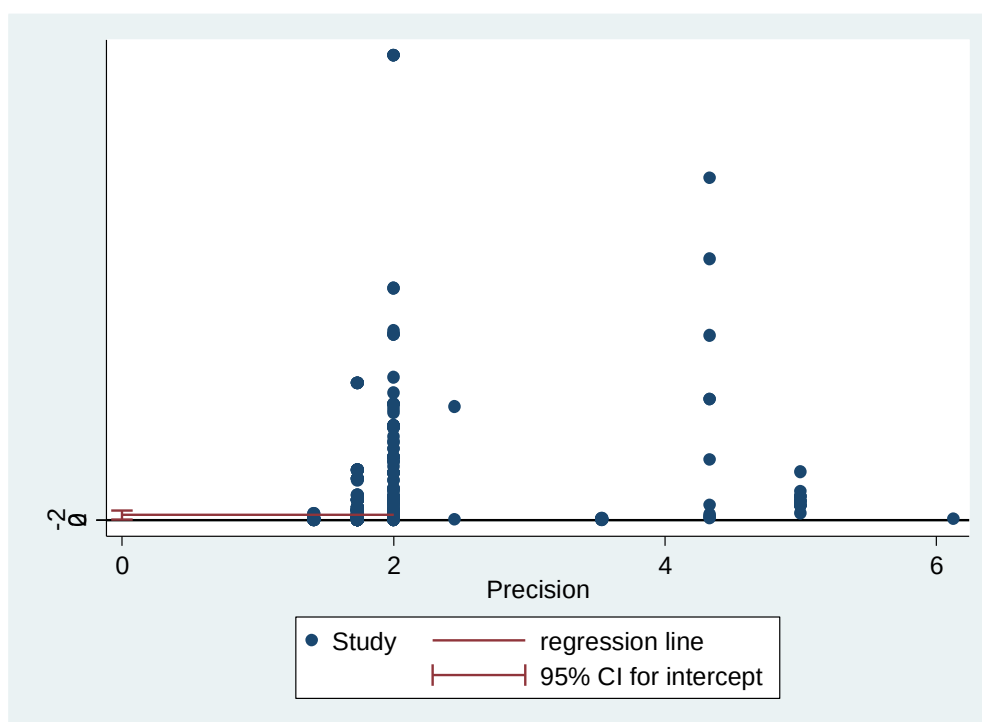


Figure 55: Metabias forest plot showing hydroacetonic-extract in 24h incubation.

The following forest plot illustrates the hydroacetic extract in 48h incubation, where the bias value is 0.000 less than 0.05, meaning that it has statistic bias.

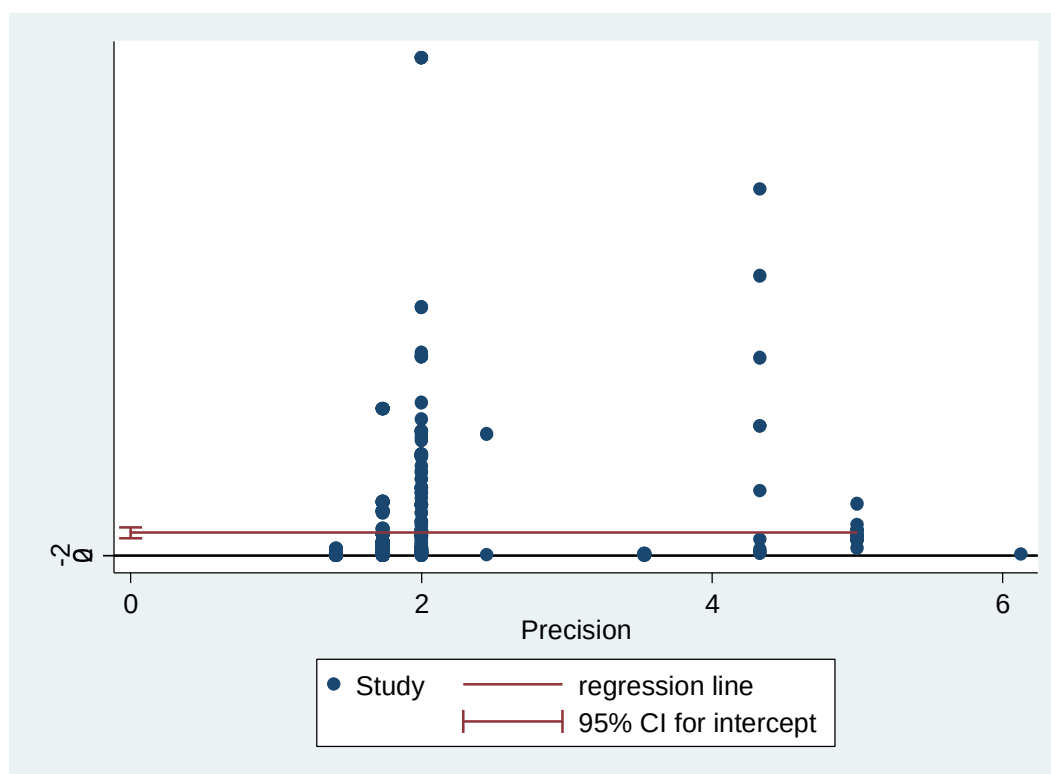


Figure 56: Metabias forest plot showing hydroacetic extract in 48h incubation.

6.2 Results of meta-analysis in classcompound1

In previous section we presented meta-analysis of classcompounds into strain and phylum. We proceeded some extra meta-analysis by order and by class of microorganisms.

At first, we observed the data from meta-analysis of random effect model of classcompound1, for different compounds and extracts during 24 and 48h incubation against different microorganisms.

6.2.1 By order

The diagrams here illustrate the meta-analysis of clasccompound1 against the stratification of microorganisms in strains.

Table 35:Results of meta-analysis process. The table illustrates MIC value along with Confidence Interval (CI), p-value after meta-analysis of classcompound1 against different strains by order stratification for 24 hours incubation. Finally, it shows the number of studies being used.

order	classcompound1	hours	number of studies	effect	confidence interval	value	df	p-value	I ²
Bacillales	xanthohumol	24	20	6,118	3,948-8,288	1964,98	19	0	99%
Lactobacillales	xanthohumol	24	14	44,395	21,192-67,597	79551	13	0	100%
Bacillales	humulone	24	17	45,5	22,301-68,698	1,80E+05	16	0	100%
Lactobacillales	humulone	24	6	40,848	22,824-58,871	17186,64	5	0	100%
Bacillales	lupulone	24	18	2,306	1,278-3,334	366,45	17	0	95,40%
Lactobacillales	lupulone	24	7	32,428	(-)0,298-65,155	26347	6	0	100%
Bacillales	cohumulone	24	4	273,75	196,821-350,679	55460,25	3	0	100%

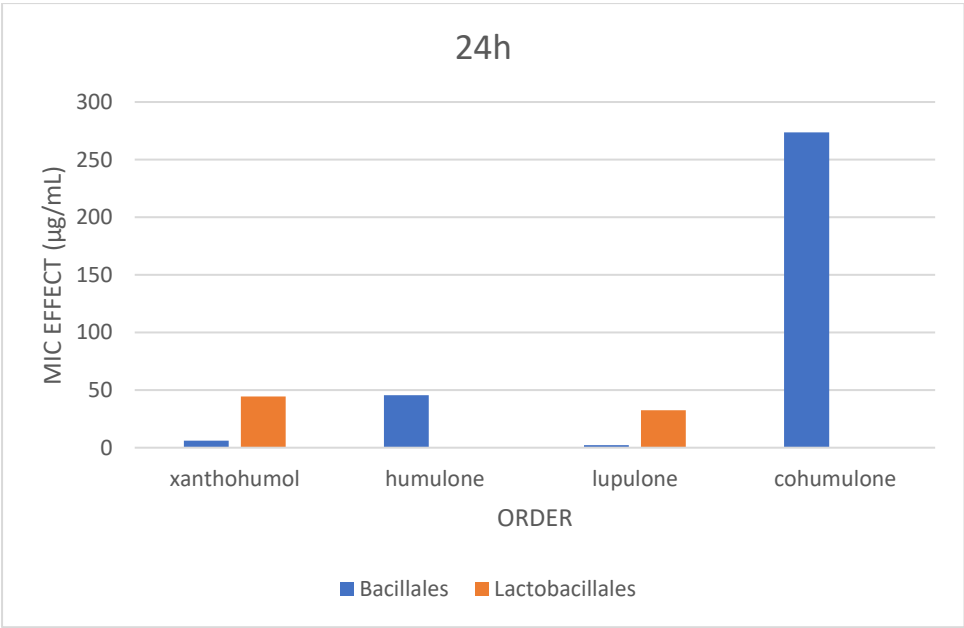


Table 36: Results of meta-analysis process. The table illustrates MIC value along with Confidence Interval (CI), p-value after meta-analysis of classcompound1 against different strains by order stratification for 24 hours incubation. Finally, it shows the number of studies being used.

order	classcompound1	hours	number of studies	effect	confidence interval	value	df	p-value	I ²
Propionibacteriales	CO2-extract	24	4	3,488	2,728- 4,247	5,41	3	0,144	44,50%
Bacillales	CO2-extract	24	11	6,648	3,349- 9,947	1017,81	10	0	100%
Lactobacillales	CO2-extract	24	8	887,5	232,725- 1542,275	4,00E+07	7	0	100%
Mycobacteriales	Hydralcoholic- extract	24	2	39	38,2-39,8	0	1	1	
Lactobacillales	Hydralcoholic- extract	24	9	66,667	37,419- 95,914	55080,71	8	0	
Bacillales	Hydralcoholic- extract	24	8	207,5	26,644- 388,356	1,40E+06	7	0	100%
Pseudomonadales	Hydralcoholic- extract	24	3	625	624,347- 625,653	0	2	1	
Saccharomycetales	Hydralcoholic- extract	24	3	273,333	(-)77,594- 624,261	5,80E+05	2	0	100%
Bacillales	Hydroacetonc- extract	24	14	55,657	12,151- 99,163	3,60E+05	13	0	100%

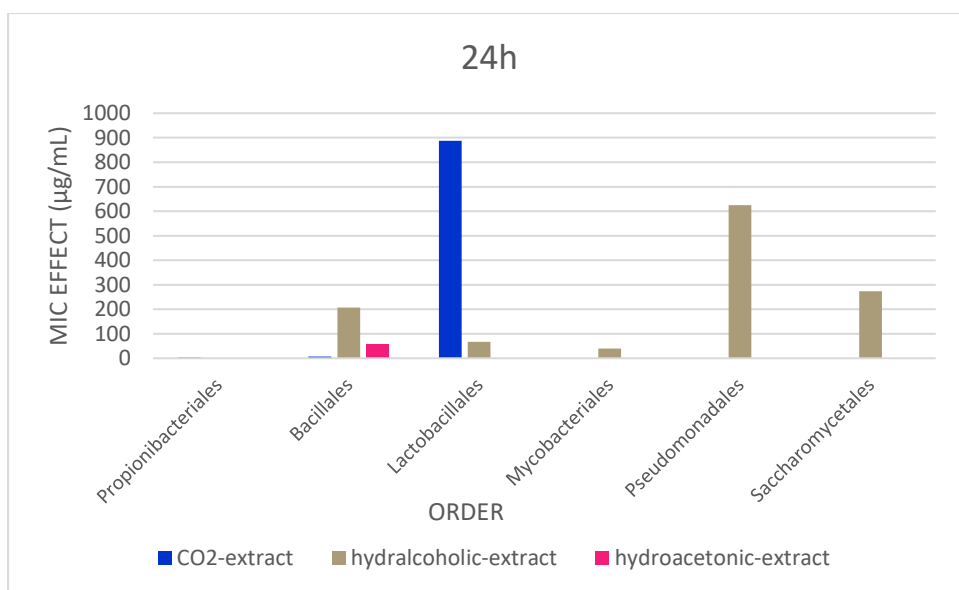


Figure 57: Minimum Inhibitory Concentration of hop extracts against microorganisms by order stratification after 24h incubation. Beige color stands for hydralcoholic-extract, pink for hydroacetic-extract, blue for CO2-extract

Table 37: Results of meta-analysis process. The table illustrates MIC value along with Confidence Interval (CI), p-value after meta-analysis of classcompound1 against different strains by order stratification for 48 hours incubation. Finally, it shows the number of studies being used.

order	classcompound1	hours	number of studies	effect	confidence interval	value	df	p-value	I ²
Bacteroidales	xanthohumol	48	7	39,429	27,795-51,062	5918,86	6	0	99,90%
Eubacteriales	xanthohumol	48	33	55,03	47,712-62,348	58883,88	32	0	99,90%
Lactobacillales	xanthohumol	48	2	0,586	(-)0,214-1,386	0,23	1	0,633	0%
Propionibacteriales	xanthohumol	48	2	46,875	16,251-77,499	1464,84	1	0	99,90%
Saccharomycetales	xanthohumol	48	3	50	30,4-69,6	2400	2	0	99,90%
Saccharomycetales	humulone	48	4	500	153,524-846,476	1,50E+06	3	0	100%
Saccharomycetales	lupulone	48	3	666,667	340,006-993,327	6,70E+05	2	0	100%
Bacillales	catechin	48	9	536,445	112,022-960,867	3,10E+07	8	0	100%
Lactobacillales	catechin	48	2	1700	1698,868-1701,132	0	1	1	

Pseudomonadales	catechin	48	2	1700	1698,868- 1701,132	0	1	1
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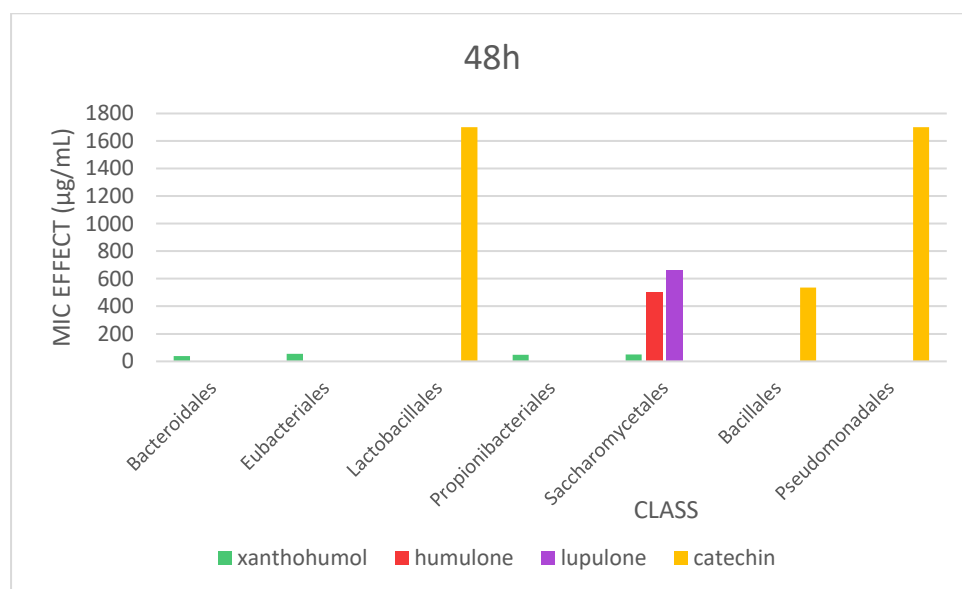


Figure 58: Minimum Inhibitory Concentration of meta-analysis for three hop compounds, against different microorganisms by order stratification after 24h incubation. Green color stands for xanthohumol, red for humulone, purple for lupulone and yellow for catechin.

Table 38: Results of meta-analysis process. The table illustrates MIC value along with Confidence Interval (CI), p-value after meta-analysis of classcompound1 against different strains by order stratification for 48 hours incubation. Finally, it shows the number of studies being used.

order	classcompound1	hours	number of studies	effect	confidence interval	value	df	p-value	I ²
Bacillales	CO2-extract	48	15	41,153	10,995-71,311	2,50E+05	14	0	100%
Enterobacteriales	CO2-extract	48	12	2604,167	1550,473-3657,86	1,50E+08	11	0	100%
Lactobacillales	CO2-extract	48	4	0,586	0,02-1,152	0,46	3	0,928	0%
Propionibacteriales	CO2-extract	48	4	15,625	15,059-16,191	0	3	1	100%
Saccharomycetales	CO2-extract	48	4	500	153,524-846,476	1,50E+06	3	0	100%
Bifidobacteriales	Hydralcoholic-extract	48	12	154,667	109,761-199,572	2,10E+05	11	0	100%
Lactobacillales	Hydralcoholic-extract	48	24	86,667	64,579-108,754	2,10E+05	23	0	100%

Fusobacteriales	Hydralcoholic-extract	48	12	250,667	154,914-346,419	9,50E+05	11	0	100%
Saccharomycetales	Hydralcoholic-extract	48	4	384	239,157-528,843	2,00E+05	3	0	100%
Lactobacillales	Hydroacetic-extract	48	14	92,257	71,858-112,656	4,90E+05	13	0	100%

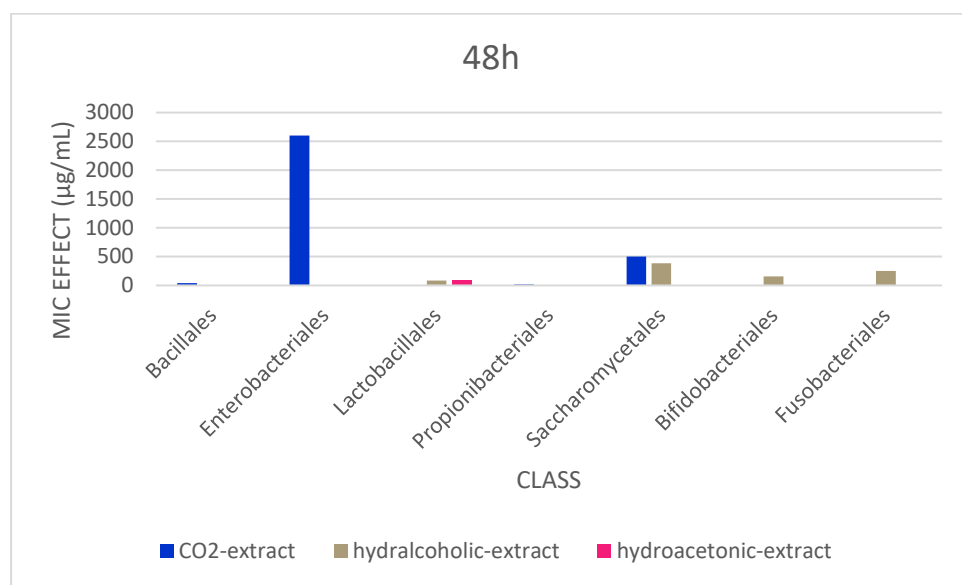


Figure 59: Minimum Inhibitory Concentration of hop extracts against microorganisms by order stratification after 48h incubation. Beige color stands for hydralcoholic-extract, pink for hydroacetic-extract, blue for CO2-extract.

6.2.2 By class

Table 39:Results of meta-analysis process. The table illustrates MIC value along with Confidence Interval (CI), p-value after meta-analysis of classcompound1 against different strains by class stratification for 24 hours incubation. Finally, it shows the number of studies being used.

class	classcompound1	hours	number of studies	effect	confidence interval	value	df	p-value	I ²
Bacilli	xanthohumol	24	34	21,881	10,438-33,323	1,50E+05	33	0	100%
Bacilli	humulone	24	23	40,848	22,824-58,871	2,00E+05	22	0	100%
Bacilli	lupulone	24	25	10,761	2,859-18,663	37241,41	24	0	100%
Bacilli	cohumulone	24	4	273,75	196,821-350,679	55460,25	3	0	100%

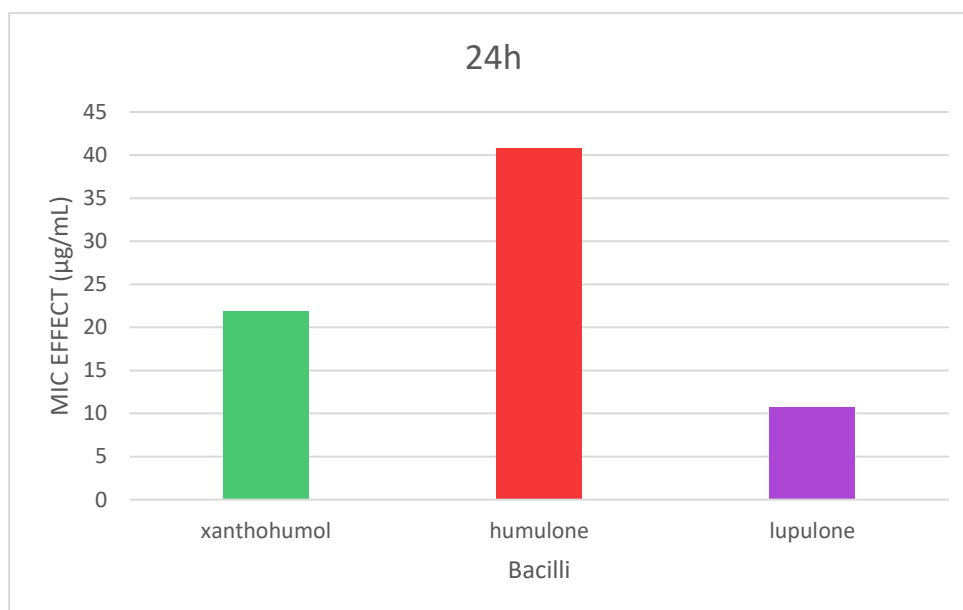


Figure 60: Minimum Inhibitory Concentration of meta-analysis for three hop compounds, against different microorganisms by class stratification after 24h incubation. Green color stands for xanthohumol, red for humulone, purple for lupulone.

Table 40: Results of meta-analysis process. The table illustrates MIC value along with Confidence Interval (CI), p-value after meta-analysis of classcompound1 against different strains by class stratification for 24 hours incubation. Finally, it shows the number of studies being used.

class	classcompound1	hours	number of studies	effect	confidence interval	value	df	p-value	I ²
Actinomycetia	CO2-extract	24	4	3,488	2,728-4,247	5,41	3	0,144	44,50%
Bacilli	CO2-extract	24	19	377,531	278,21-2448,562	5,10E+08	18	0	100%
Actinomycetia	Hydralcoholic-extract	24	2	39	38,2-39,8	0	1	1	
Bacilli	Hydralcoholic-extract	24	17	132,941	45,341-220,542	1,80E+06	16	0	100%
Gammaproteobacteria	Hydralcoholic-extract	24	4	625	624,434-625,566	0	3	1	
Saccharomycetes	Hydralcoholic-extract	24	3	273,333	120,96-314,271	5,80E+05	2	0	100%
Actinomycetia	Hydralcoholic-extract	24	12	154,667	109,761-199,572	2,10E+05	11	0	100%
Bacilli	Hydroacetonc-extract	24	14	55,657	12,151-99,163	3,60E+05	13	0	100%

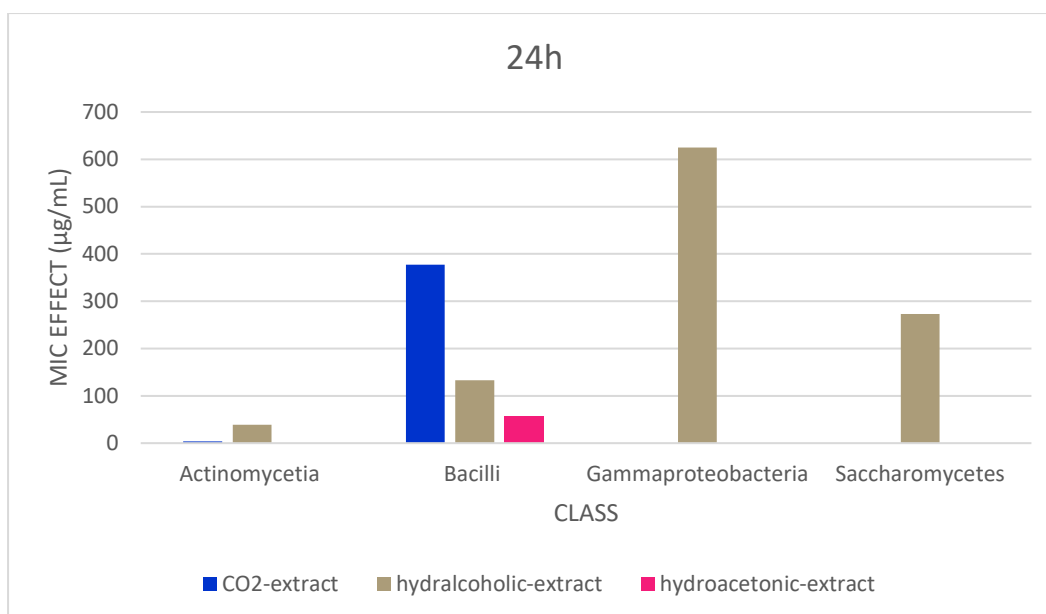


Figure 61: Minimum Inhibitory Concentration of hop extracts against microorganisms by class stratification after 24h incubation. Beige color stands for hydralcoholic-extract, pink for hydroacetic-extract, blue for CO2-extract.

Table 41: Results of meta-analysis process. The table illustrates MIC value along with Confidence Interval (CI), p-value after meta-analysis of classcompound1 against different strains by class stratification for 48 hours incubation. Finally, it shows the number of studies being used.

class	classcompound1	hours	number of studies	effect	confidence interval	value	df	p-value	I ²
Bacteroida	xanthohumol	48	7	39,429	27,759-51,062	5918,86	6	0	99,90%
Clostridia	xanthohumol	48	33	55,03	47,712-62,348	58883,88	32	0	99,90%
Bacilli	xanthohumol	48	2	0,586	(-)0,214-1,386	0,23	1	0,633	0%
Actinomycetia	xanthohumol	48	2	46,875	16,251-77,499	1464,84	1	0	99,90%
Saccharomycetes	xanthohumol	48	3	50	30,4-69,6	2400	2	0	99,90%
Saccharomycetes	humulone	48	4	500	153,524-846,476	1,50E+06	3	0	100%
Saccharomycetes	lupulone	48	3	666,667	340,006-993,327	6,70E+05	2	0	100%
Bacilli	catechin	48	11	748	357,12-1138,88	3,50E+07	10	0	100%
Gammaproteobacteria	catechin	48	2	1700	1699,2-1700,8	0	1	1	

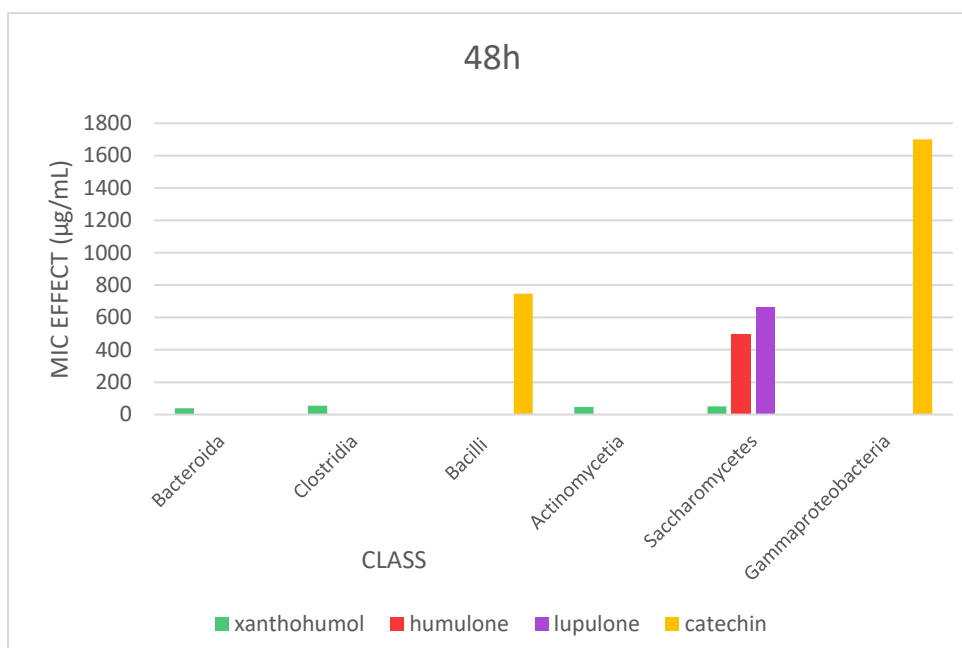


Figure 62: Minimum Inhibitory Concentration of meta-analysis for three hop compounds, against different microorganisms after 48h incubation. Green color stands for xanthohumol, red for humulone, purple for lupulone and yellow for catechin.

Table 42: Results of meta-analysis process. The table illustrates MIC value along with Confidence Interval (CI), p-value after meta-analysis of classcompound1 against different strains by class stratification for 48 hours incubation. Finally, it shows the number of studies being used.

class	classcompound1	hours	number of studies	effect	confidence interval	value	df	p-value	I ²
Bacilli	CO2-extract	48	19	32,613	7,247-57,979	2,70E+05	18	0	100%
Gammaproteobacteria	CO2-extract	48	12	2604,167	1550,473-3657,86	1,50E+08	11	0	100%
Actinomycetia	CO2-extract	48	4	15,625	15,059-16,191	0	3	0	100%
Saccharomycetes	CO2-extract	48	4	500	153,524-846,476	1,50E+06	3	0	100%
Bacilli	Hydralcoholic-extract	48	24	86,667	64,579-108,754	2,10E+05	23	0	100%
Fusobacteriia	Hydralcoholic-extract	48	12	250,667	154,914-346,419	9,5e_05	11	0	100%
Saccharomycetes	Hydralcoholic-extract	48	4	384	239,157-528,843	2,00E+05	3	0	100%
Bacilli	Hydroacetonc-extract	48	14	92,257	71,858-112,656	4,90E+05	13	0	100%

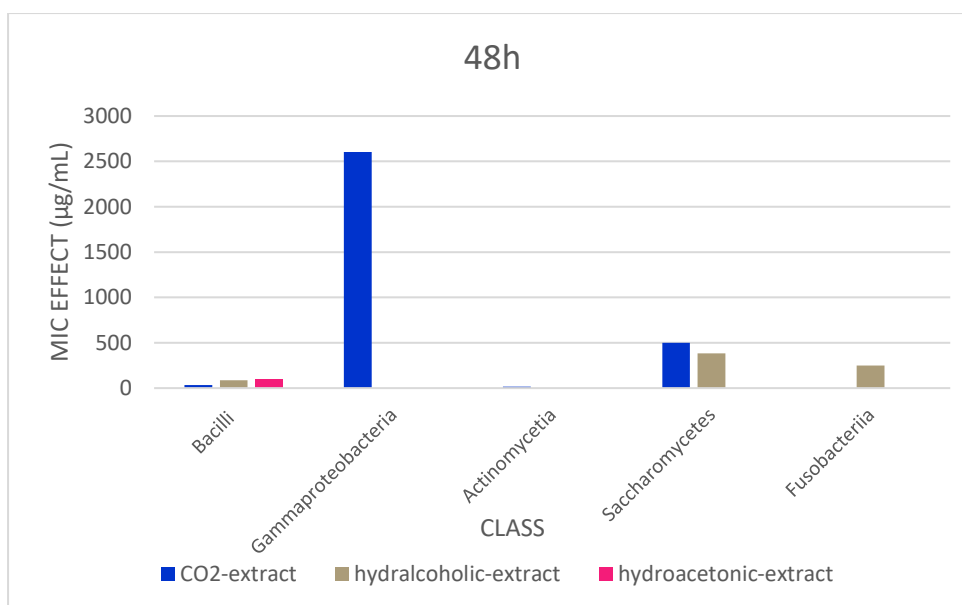


Figure 63: Minimum Inhibitory Concentration of hop extracts against microorganisms after 48h incubation. Beige color stands for hydralcoholic-extract, pink for hydroacetic-extract, blue for CO2-extract.

6.3 Results of meta-analysis in classcompound2

6.3.1 By order

Table 43: Results of meta-analysis process. The table illustrates MIC value along with Confidence Interval (CI), p-value after meta-analysis of classcompound2 against different strains by order stratification for 24 hours incubation. Finally, it shows the number of studies being used.

order	classcompound2	hours	number of studies	effect	confidence interval	value	df	p-value	I ²
Bacillales	chalcones	24	25	10,449	6,216-14,681	11188,31	24	0	99,80%
Lactobacillales	chalcones	24	14	44,395	21,192-67,597	79551	13	0	100%
Bacillales	α-acids	24	26	112,481	5,837-219,125	1,40E+07	25	0	100%
Lactobacillales	α-acids	24	6	27,668	3,565-51,77	17186,64	5	0	100%
Bacillales	β-acids	24	23	12,027	3,611-20,442	38488,6	22	0	99,90%
Lactobacillales	β-acids	24	7	32,428	(-)0,298-65,155	26347	6	0	100%

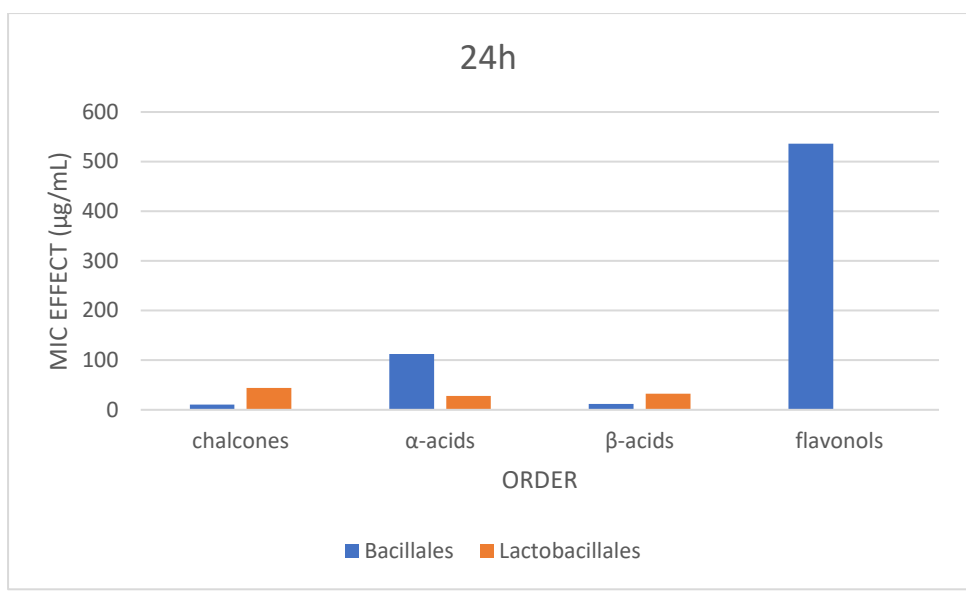


Table 44: Results of meta-analysis process. The table illustrates MIC value along with Confidence Interval (CI), p-value after meta-analysis of classcompound2 against different strains by class stratification for 24 hours incubation. Finally, it shows the number of studies being used.

order	classcompound2	hours	number of studies	effect	confidence interval	value	df	p-value	I ²
Propionibacteriales	CO2-extract	24	4	3,488	2,728-4,247	5,41	3	0,144	44,50%
Bacillales	CO2-extract	24	11	6,648	3,349-9,947	1017,81	10	0	100%
Lactobacillales	CO2-extract	24	8	887,5	232,725-1542,275	4,00E+07	7	0	100%
Mycobacteriales	hydralcoholic-extract	24	2	39	38,2-39,8	0	1	1	
Lactobacillales	hydralcoholic-extract	24	9	66,667	37,419-95,914	55080,71	8	0	100%
Bacillales	hydralcoholic-extract	24	8	207,5	26,644-388,356	1,40E+06	7	0	100%
Pseudomonadales	hydralcoholic-extract	24	3	625	624,247-625,653	0	2	1	
Saccharomycetales	hydralcoholic-extract	24	3	273,333	(-)77,594-624,261	5,80E+05	2	0	100%
Bacillales	hydroacetic-extract	24	14	55,657	12,151-99,163	3,60E+05	13	0	100%

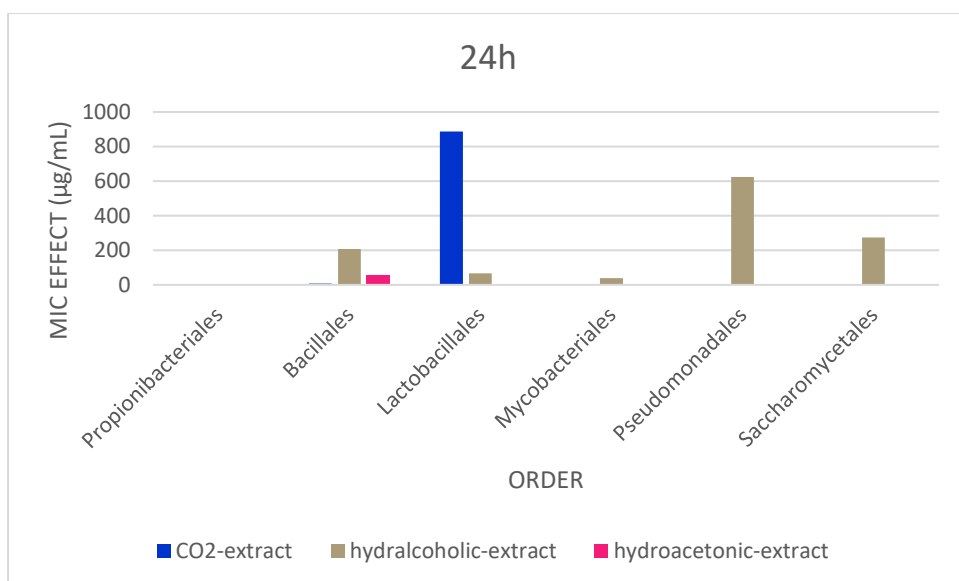


Figure 64: Minimum Inhibitory Concentration of hop extracts against microorganisms by order stratification after 24h incubation. Beige color stands for hydralcoholic-extract, pink for hydroacetic-extract, blue for CO2-extract.

Table 45: Results of meta-analysis process. The table illustrates MIC value along with Confidence Interval (CI), p-value after meta-analysis of classcompound2 against different strains by order stratification for 48 hours incubation. Finally, it shows the number of studies being used.

order	classcompound2	hours	number of studies	effect	confidence interval	value	df	p-value	I ²
Bacillales	chalcones	48	6	5,7	2,77-8,63	268,16	5	0	98,10%
Enterobacteriales	chalcones	48	6	200	199,6-200,4	0	5	1	
Bacteroidales	chalcones	48	7	39,429	27,795-51,062	5918,86	6	0	99,90%
Eubacteriales	chalcones	48	33	55,03	47,712-62,348	58883,88	32	0	99,90%
Lactobacillales	chalcones	48	2	0,586	(-)0,214-1,386	0,23	1	0,633	0%
Propionibacteriales	chalcones	48	2	46,875	16,251-77,499	1464,84	1	0	99,90%
Saccharomycetales	chalcones	48	3	50	30,4-69,6	2400	2	0	99,90%
Bacteroidales	α-acids	48	7	767,143	408,979-1125,307	5,60E+06	6	0	100%
Eubacteriales	α-acids	48	33	786,364	661,831-910,896	1,70E+07	32	0	100%
Saccharomycetales	α-acids	48	4	500	153,524-846,476	1,50E+06	3	0	100%
Bacteroidales	β-acids	48	7	258,571	168,102-349,041	3,60E+05	6	0	100%

Eubacteriales	β -acids	48	33	62,97	41,339-84,6	5,10E+05	32	0	100%
Saccharomycetales	β -acids	48	3	666,667	340,006-993,327	6,70E+05	2	0	100%
Bacillales	flavonols	48	9	536,445	112,022-960,867	3,10E+07	8	0	100%
Lactobacillales	flavonols	48	2	1700	1699,2-1700,8	0	1	1	
Pseudomonadales	flavonols	48	2	1700	1699,2-1700,8	0	1	1	

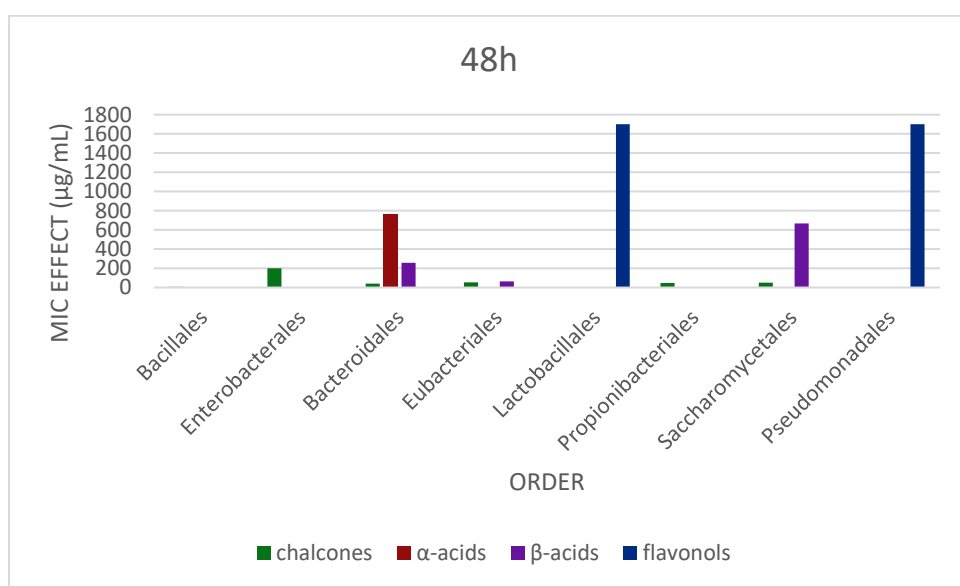


Figure 65: Minimum Inhibitory Concentration of meta-analysis of hop compounds' classes against microorganisms' classes after 48h incubation. Red stands for α -acids, purple for β -acids, blue for flavonols and green for chalcones.

Table 46: Results of meta-analysis process. The table illustrates MIC value along with Confidence Interval (CI), p-value after meta-analysis of classcompound2 against different strains by order stratification for 48 hours incubation. Finally, it shows the number of studies being used.

order	classcompound2	hours	number of studies	effect	confidence interval	value	df	p-value	I ²
Bacillales	CO2-extract	48	15	41,153	10,995-71,311	2,50E+05	14	0	100%
Enterobacteriales	CO2-extract	48	12	2604,167	1550,473-3657,86	1,50E+08	11	0	100%
Lactobacillales	CO2-extract	48	4	0,586	0,020-1,152	0,46	3	0,928	0%
Propionibacteriales	CO2-extract	48	4	15,625	15,059-16,191	0	3	1	100%
Saccharomycetales	CO2-extract	48	4	500	153,524-846,476	1,50E+06	3	0	100%

Bifidobacteriales	hydralcoholic-extract	48	12	154,667	109,761-199,572	2,10E+05	11	0	100%
Lactobacillales	hydralcoholic-extract	48	24	86,667	64,579-108,754	2,10E+05	23	0	100%
Fusobacteriales	hydralcoholic-extract	48	12	250,667	154,914-346,419	9,50E+05	11	0	100%
Saccharomycetales	hydralcoholic-extract	48	4	384	239,157-528,843	2,00E+05	3	0	100%
Lactobacillales	hydroacetic-extract	48	14	92,257	71,858-112,656	4,90E+05	13	0	100%

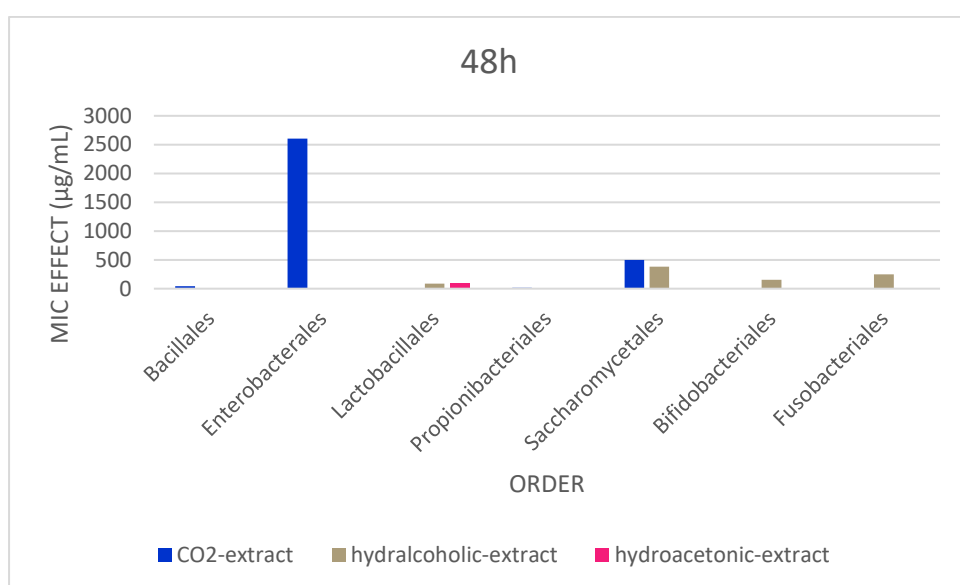


Figure 66: Minimum Inhibitory Concentration of hop extracts against microorganisms after 48h incubation. Beige color stands for hydralcoholic-extract, pink for hydroacetic-extract, blue for CO2-extract.

6.3.2 By class

Table 47: Results of meta-analysis process. The table illustrates MIC value along with Confidence Interval (CI), p-value after meta-analysis of classcompound2 against different strains by class stratification for 24 hours incubation. Finally, it shows the number of studies being used.

class	classcompound2	hours	number of studies	effect	confidence interval	value	df	p-value	I ²
Bacilli	chalcones	24	39	22,635	12,419-32,852	1,50E+05	38	0	100%
Bacilli	α-acids	24	32	96,578	6,035-187,122	1,40E+07	31	0	100%
Bacilli	β-acids	24	30	16,786	7,581-25,992	71051,75	29	0	100%

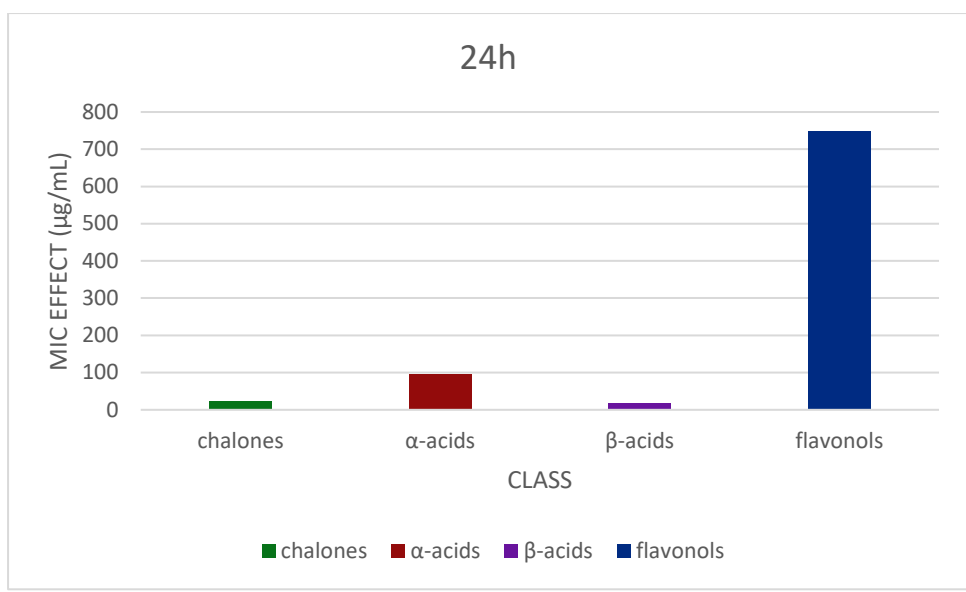


Figure 67: Minimum Inhibitory Concentration of meta-analysis of hop compounds' classes against microorganisms' classes by class stratification after 24h incubation. Red stands for α -acids, purple for β -acids, blue for flavonols and green for chalcones.

Table 48: Results of meta-analysis process. The table illustrates MIC value along with Confidence Interval (CI), p-value after meta-analysis of classcompound2 against different strains by class stratification for 24 hours incubation. Finally, it shows the number of studies being used.

class	classcompound2	hours	number of studies	effect	confidence interval	value	df	p-value	I ²
Actinomycetia	CO2-extract	24	4	3,488	2,728-4,247	5,41	3	0,144	44,50%
Bacilli	CO2-extract	24	19	377,531	278,21-2448,562	5,10E+08	18	0	100%
Actinomycetia	hydralcoholic-extract	24	2	39	38,2-39,8	0	1	1	
Bacilli	hydralcoholic-extract	24	17	132,941	45,341-220,542	1,80E+06	16	0	100%
Gammaproteobacteria	hydralcoholic-extract	24	4	625	624,434-625,566	0	3	1	
Saccharomycetes	hydralcoholic-extract	24	3	273,333	(-)77,594=624,261	5,80E+05	2	0	100%
Bacilli	hydroacetonc-extract	24	14	55,657	12,151-99,163	3,60E+05	13	0	100%

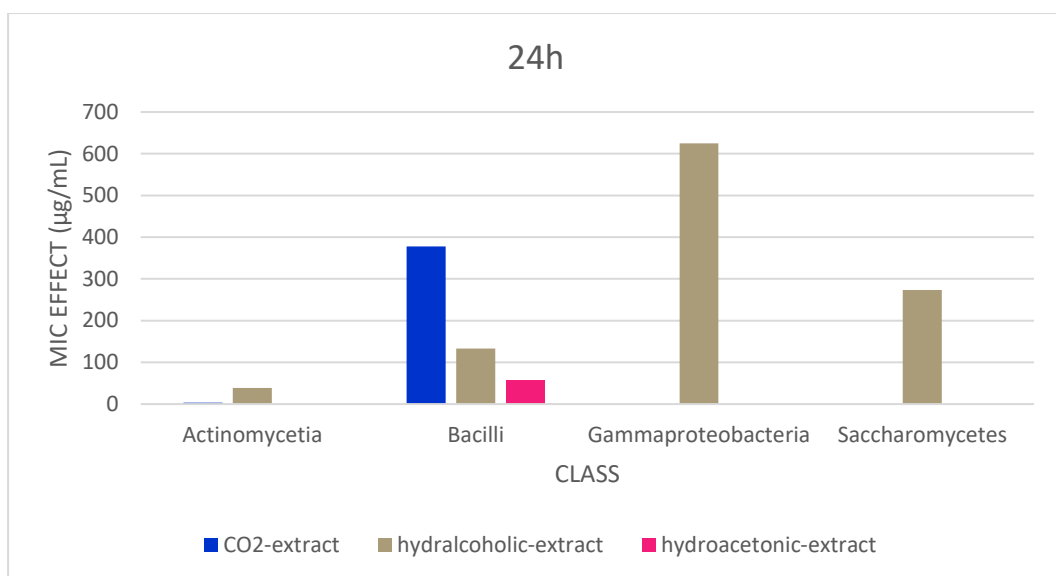


Figure 68: Minimum Inhibitory Concentration of hop extracts against microorganisms after 24h incubation. Beige color stands for hydralcoholic-extract, pink for hydroacetic-extract, blue for CO2-extract.

Table 49: Results of meta-analysis process. The table illustrates MIC value along with Confidence Interval (CI), p-value after meta-analysis of classcompound2 against different strains by class stratification for 48 hours incubation. Finally, it shows the number of studies being used.

class	classcompound2	hours	number of studies	effect	confidence interval	value	df	p-value	I ²
Bacilli	chalcones	48	8	4,427	1,74-7,114	393,92	7	0	98,20%
Gammaproteobacteria	chalcones	48	6	200	199,6-200,4	0	5	1	
Bacteroida	chalcones	48	7	39,429	27,795-51,062	5918,86	6	0	99,90%
Clostridia	chalcones	48	33	55,03	47,712-62,348	58883,88	32	0	99,90%
Actinomycetia	chalcones	48	2	46,875	16,251-77,499	1464,84	1	0	99,90%
Saccharomycetes	chalcones	48	3	50	30,4-69,6	2400	2	0	99,90%
Bacteroida	α-acids	48	7	767,143	408,979-1125,307	5,60E+06	6	0	100%
Clostridia	α-acids	48	33	786,364	661,831-910,896	1,70E+07	32	0	100%
Saccharomycetes	α-acids	48	4	500	153,524-846,476	1,50E+06	3	0	100%
Bacteroida	β-acids	48	7	258,571	168,102-349,041	3,60E+05	6	0	100%
Clostridia	β-acids	48	33	62,97	41,339-84,6	5,10E+05	32	0	100%

Saccharomycetes	β -acids	48	3	666,667	340,006-993,327	6,70E+05	2	0	100%
Bacilli	flavonols	48	11	748	357,12-1138,88	3,50E+07	10	0	100%
Gammaproteobacteria	flavonols	48	2	1700	1699,2-1700,8	0	1	0	100%

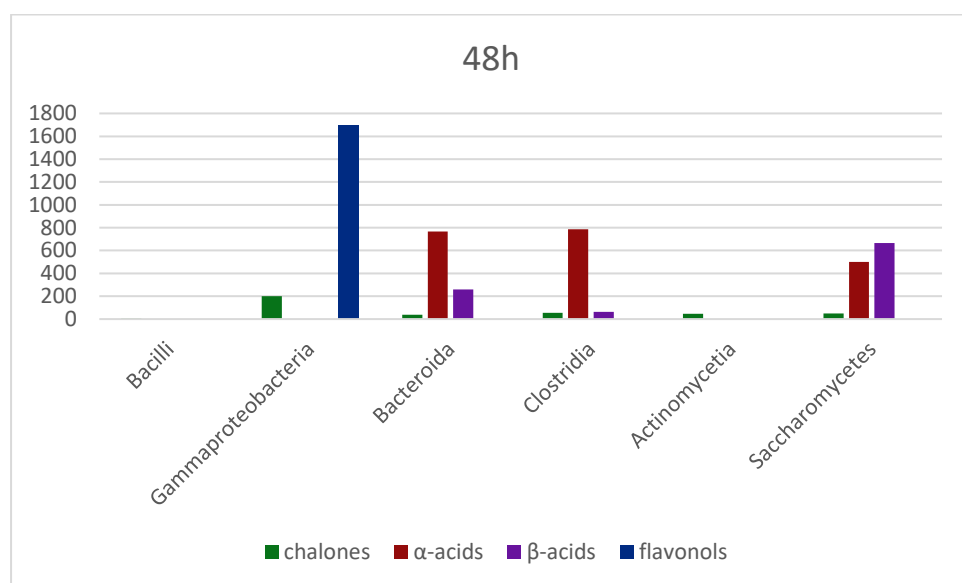


Figure 69: Minimum Inhibitory Concentration of meta-analysis of hop compounds' classes against microorganisms' classes after 48h incubation. Red stands for α -acids, purple for β -acids, blue for flavonols and green for chalcones.

Table 50: Results of meta-analysis process. The table illustrates MIC value along with Confidence Interval (CI), p-value after meta-analysis of classcompound2 against different strains by class stratification for 48 hours incubation. Finally, it shows the number of studies being used.

class	classcompound2	hours	number of studies	effect	confidence interval	value	df	p-value	I ²
Bacilli	CO2-extract	48	19	32,613	7,247-57,979	2,70E+05	18	0	100%
Gammaproteobacteria	CO2-extract	48	12	2604,167	1550,473-3657,86	1,50E+08	11	0	100%
Actinomycetia	CO2-extract	48	4	15,625	15,059-16,191	0	3	0	100%
Saccharomycetes	CO2-extract	48	4	500	153,524-846,476	1,50E+06	3	0	100%
Actinomycetia	hydralcoholic-extract	48	12	154,667	109,761-199,572	2,10E+05	11	0	100%
Bacilli	hydralcoholic-extract	48	24	86,667	64,579-108,754	2,10E+05	23	0	100%

Fusobacteriia	hydralcoholic-extract	48	12	250,667	154,914-346,419	9,50E+05	11	0	100%
Saccharomycetes	hydralcoholic-extract	48	4	384	239,157-528,843	2,00E+05	3	0	100%
Bacilli	hydroacetonic-extract	48	14	92,257	71,858-112,656	4,90E+05	13	0	100%

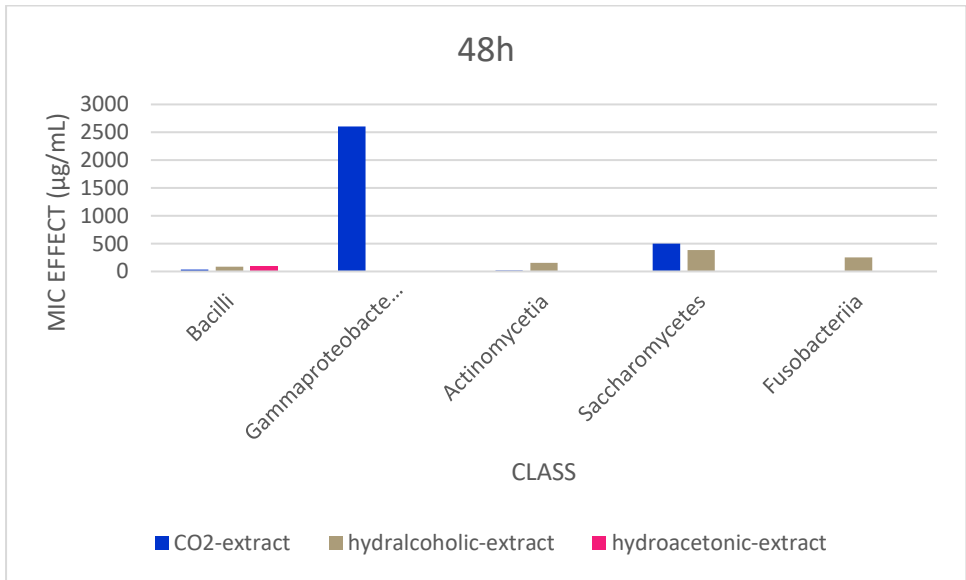


Figure 70: Minimum Inhibitory Concentration of hop extracts against microorganisms after 48h incubation. Beige color stands for hydralcoholic-extract, pink for hydroacetonic-extract, blue for CO2-extract.

6.4 Results of meta-analysis in classcompound3

6.4.1 By order

Table 51: Results of meta-analysis process. The table illustrates MIC value along with Confidence Interval (CI), p-value after meta-analysis of classcompound3 against different strains by order classification for 48 hours incubation. Finally, it shows the number of studies being used.

order	classcompound3	hours	number of studies	effect	confidence interval	value	df	p-value	I ²
Bacillales	flavonoids	24	25	10,449	6,216-14,681	11188,31	24	0	99,80%
Lactobacillales	flavonoids	24	14	44,395	21,192-67,597	79551	13	0	100%
Bacillales	bitter acids	24	49	65,329	0,76-129,898	1,50E+07	48	0	100%
Lactobacillales	bitter acids	24	13	30,231	11,426-49,035	44091,29	12	0	100%

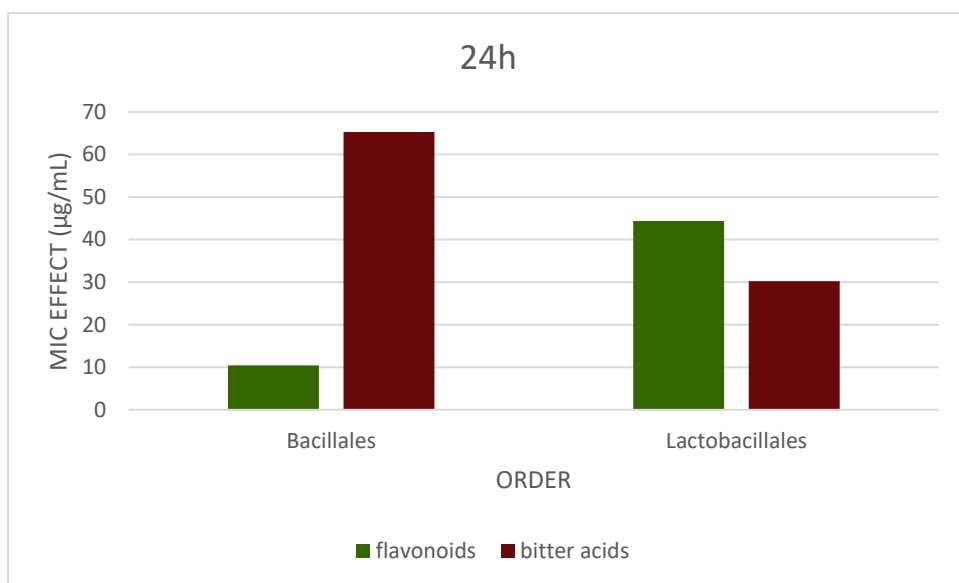


Figure 71: Minimum Inhibitory Concentration of meta-analysis of hop compounds' classes against microorganisms after 24h incubation. Green color stands for flavonoids and dark red for bitter acids.

Table 52: Results of meta-analysis process. The table illustrates MIC value along with Confidence Interval (CI), p-value after meta-analysis of classcompound3 against different strains by order classification for 24 hours incubation. Finally, it shows the number of studies being used.

order	classcompound3	hours	number of studies	effect	confidence interval	value	df	p-value	I ²
Propionibacteriales	CO2-extract	24	4	3,488	2,728-4,247	5,41	3	0,144	44,50%
Bacillales	CO2-extract	24	11	6,648	3,349-9,947	1017,81	10	0	100%
Lactobacillales	CO2-extract	24	8	887,5	232,725-1542,275	4,00E+07	7	0	100%
Mycobacteriales	hydralcoholic-extract	24	2	39	38,2-39,8	0	1	1	
Lactobacillales	hydralcoholic-extract	24	9	66,667	37,419-95,914	55080,71	8	0	100%
Bacillales	hydralcoholic-extract	24	8	207,5	26,644-388,356	1,40E+06	7	0	100%
Pseudomonadales	hydralcoholic-extract	24	3	625	624,347-625,653	0	2	1	
Saccharomycetales	hydralcoholic-extract	24	3	273,333	(-)-77,594-624,261	5,80E+05	2	0	100%

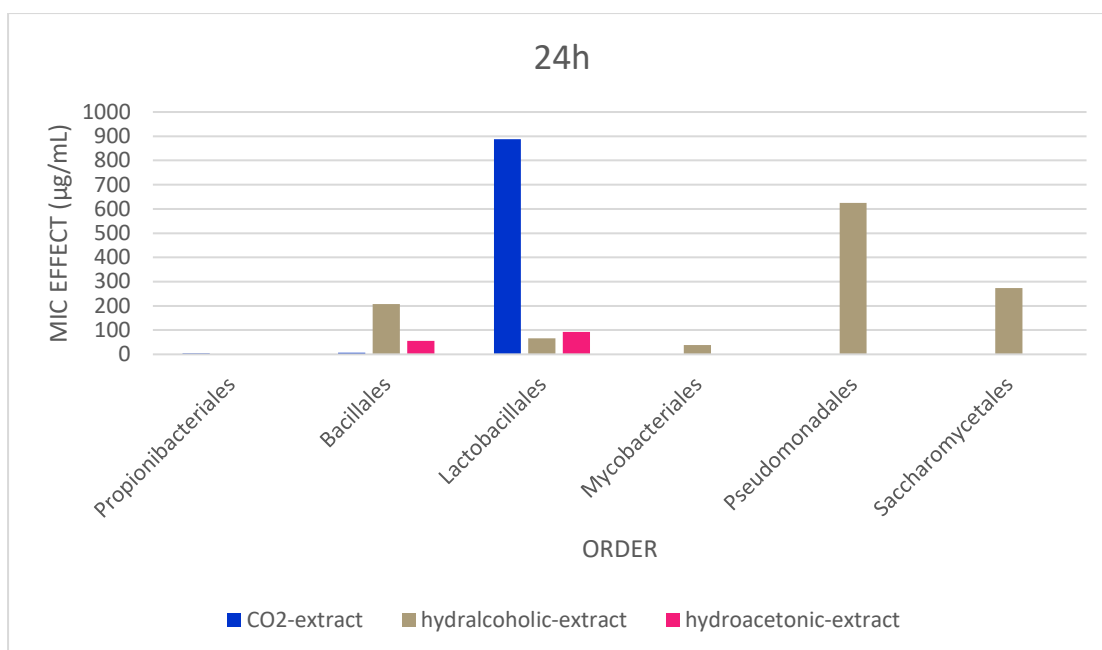


Figure 72: Minimum Inhibitory Concentration of hop extracts against microorganisms after 24h incubation. Beige color stands for hydralcoholic-extract, pink for hydroacetonc-extract, blue for CO2-extract.

Table 53: Results of meta-analysis process. The table illustrates MIC value along with Confidence Interval (CI), p-value after meta-analysis of classcompound3 against different strains by order stratification for 48 hours incubation. Finally, it shows the number of studies being used.

order	classcompound3	hours	number of studies	effect	confidence interval	value	df	p-value	I ²
Bacillales	flavonoids	48	15	324,147	(-)12,623-660,917	4,40E+07	14	0	100%
Enterobacteriales	flavonoids	48	6	200	199,6-200,4	0	5	1	
Bacteroidales	flavonoids	48	7	39,429	27,795-51,062	5918,86	6	0	99,90%
Eubacteriales	flavonoids	48	33	55,03	47,712-62,348	5,89E+04	32	0	99,90%
Lactobacillales	flavonoids	48	4	850,293	(-)111,223-1811,809	8,70E+06	3	0	100%
Propionibacteriales	flavonoids	48	2	46,875	16,251-77,499	1464,84	1	0	99,90%
Pseudomonadales	flavonoids	48	2	1700	1699,2-1700,8	0	1	1	
Bacteroidales	bitter acids	48	14	512,857	287,914-737,8	9,60E+06	13	0	100%
Eubacteriales	bitter acids	48	66	424,667	316,665-532,668	5,20E+07	65	0	100%
Saccharomycetales	bitter acids	48	7	571,429	339,269-803,588	2,40E+06	6	0	100%

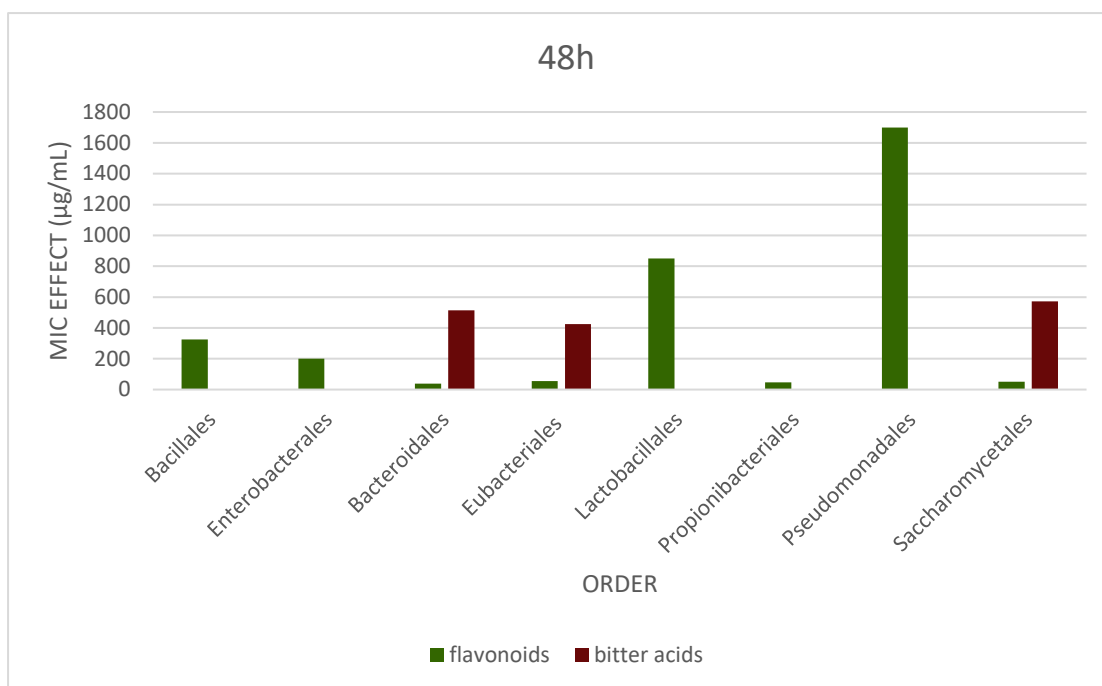


Figure 73: Minimum Inhibitory Concentration of meta-analysis of hop compounds' classes against microorganisms after 48h incubation. Green color stands for flavonoids and dark red for bitter acids.

Table 54: Results of meta-analysis process. The table illustrates MIC value along with Confidence Interval (CI), p-value after meta-analysis of classcompound3 against different strains by order stratification for 48 hours incubation. Finally, it shows the number of studies being used.

order	classcompound3	hours	number of studies	effect	confidence interval	value	df	p-value	I ²
Bacillales	CO2-extract	48	15	41,153	10,995-71,311	2,50E+05	14	0	100%
Enterobacteriales	CO2-extract	48	12	2604,167	1550,473-3657,86	1,50E+08	11	0	100%
Lactobacillales	CO2-extract	48	4	0,586	0,02-1,152	0,46	3	0,928	0%
Propionibacteriales	CO2-extract	48	4	15,625	15,059-16,191	0	3	1	100%
Saccharomycetales	CO2-extract	48	4	500	153,524-846,476	1,50E+06	3	0	100%
Bifidobacteriales	hydralcoholic-extract	48	12	154,667	109,761-199,572	2,10E+05	11	0	100%
Lactobacillales	hydralcoholic-extract	48	24	86,667	64,579-108,754	2,10E+05	23	0	100%
Fusobacteriales	hydralcoholic-extract	48	12	250,667	154,914-346,419	9,50E+05	11	0	100%
Saccharomycetales	hydralcoholic-extract	48	4	384	239,157-528,843	2,00E+05	3	0	100%

Bacillales	hydroacetic- extract	48	14	55,657	12,151- 99,163	3,60E+05	13	0	100%
Lactobacillales	hydroacetic- extract	48	14	92,257	71,858- 112,656	4,90E+05	13	0	100%

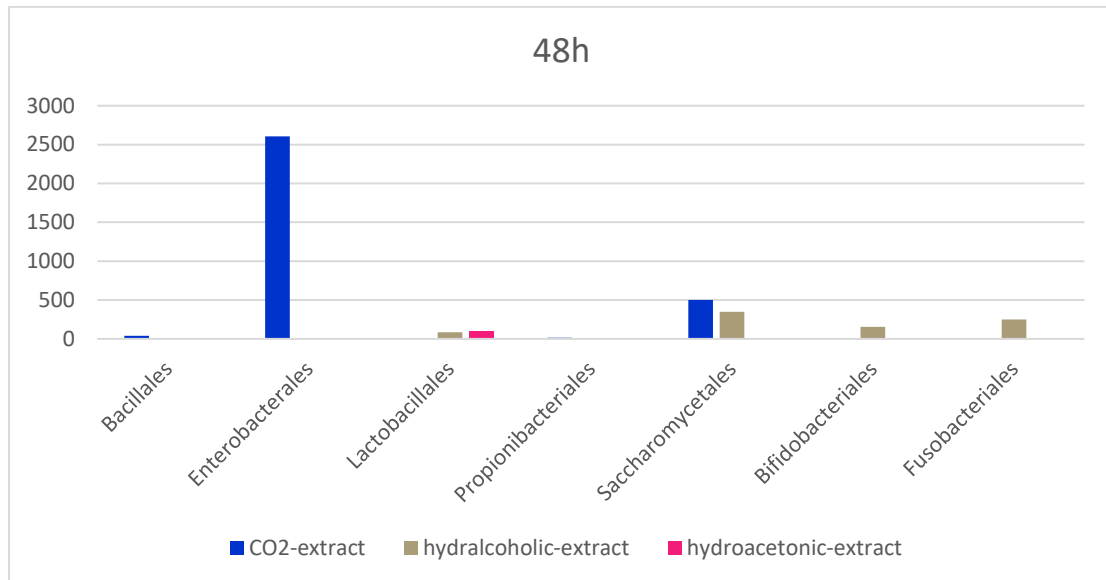


Figure 74: Minimum Inhibitory Concentration of hop extracts against microorganisms after 48h incubation. Beige color stands for hydralcoholic-extract, pink for hydroacetic-extract, blue for CO2-extract.

6.4.2 By class

Table 55: Results of meta-analysis process. The table illustrates MIC value along with Confidence Interval (CI), p-value after meta-analysis of classcompound3 against different strains by class stratification for 24 hours incubation. Finally, it shows the number of studies being used.

class	classcompound3	hours	number of studies	effect	confidence interval	value	df	p-value	I ²
Bacilli	flavonoids	24	39	22,635	12,419- 32,852	1,50E+05	38	0	100%
Bacilli	bitter acids	24	62	57,97	4,187- 111,572	1,50E+07	61	0	100%

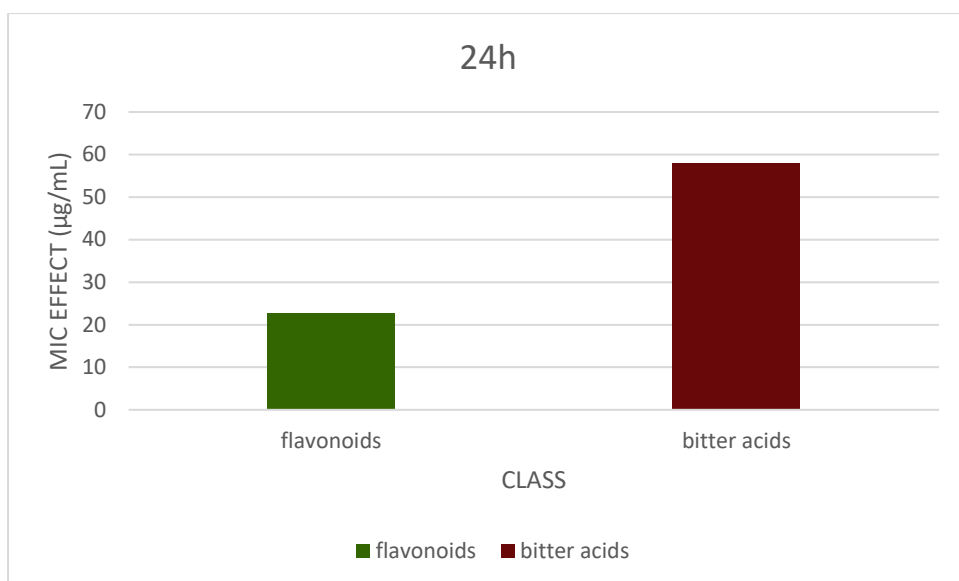


Figure 75: Minimum Inhibitory Concentration of meta-analysis of hop compounds' classes against microorganisms after 24h incubation. Green color stands for flavonoids and dark red for bitter acids.

Table 56: Results of meta-analysis process. The table illustrates MIC value along with Confidence Interval (CI), p-value after meta-analysis of classcompound3 against different strains by class stratification for 24 hours incubation. Finally, it shows the number of studies being used.

class	classcompound3	hours	number of studies	effect	confidence interval	value	df	p-value	I ²
Bacilli	flavonoids	48	19	434,914	126,106-743,723	5,40E+07	18	0	100%
Gammaproteobacteria	flavonoids	48	8	575	130,098-1019,902	1,10E+07	7	0	100%
Bacteroidia	flavonoids	48	7	39,429	27,795-51,062	5918,86	6	0	100%
Clostridia	flavonoids	48	33	55,03	47,712-62,348	58882,88	32	0	99,90%
Actinomycetia	flavonoids	48	2	46,875	16,251-77,499	1464,84	1	0	99,90%
Saccharomycetes	flavonoids	48	3	50	30,4-69,6	2400	2	0	99,90%
Bacteroidia	bitter acids	48	14	512,857	287,914-737,8	9,60E+06	13	0	100%
Clostridia	bitter acids	48	66	424,667	316,665-532,668	5,20E+07	65	0	100%
Saccharomycetes	bitter acids	48	7	571,429	339,269-803,588	2,40E+06	6	0	100%

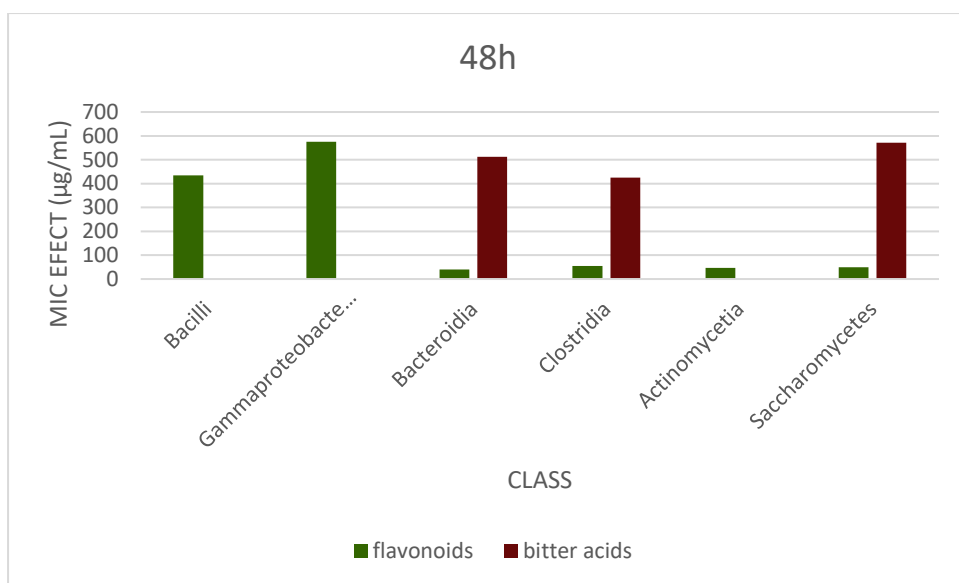


Figure 76: Minimum Inhibitory Concentration of meta-analysis of hop compounds' classes against microorganisms after 48h incubation. Green color stands for flavonoids and dark red for bitter acids.

Table 57: Results of meta-analysis process. The table illustrates MIC value along with Confidence Interval (CI), p-value after meta-analysis of classcompound3 against different strains by class stratification for 24 hours incubation. Finally, it shows the number of studies being used.

class	classcompound3	hours	number of studies	effect	confidence interval	value	df	p-value	I ²
Actinomycetia	CO2-extract	24	4	3,488	2,728-4,247	5,41	3	0,144	44,50%
Bacilli	CO2-extract	24	19	377,531	278,21-2448,562	5,10E+08	18	0	100%
Actinomycetia	hydralcoholic-extract	24	2	39	38,2-39,8	0	1	1	
Bacilli	hydralcoholic-extract	24	17	132,941	45,341-220,542	1,80E+06	16	0	100%
Gammaproteobacteria	hydralcoholic-extract	24	4	625	624,434-625,566	0	3	1	
Saccharomycetes	hydralcoholic-extract	24	3	273,333	(-)-77,594-624,621	5,80E+05	2	0	100%
Bacilli	hydroacetonc-extract	24	14	55,657	12,151-99,163	3,60E+05	13	0	100%

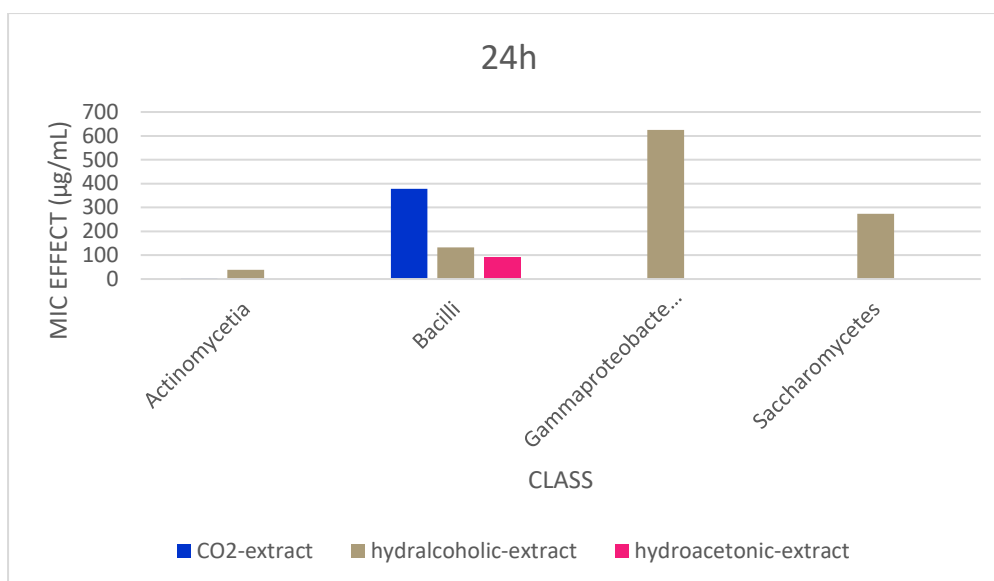


Figure 77: Minimum Inhibitory Concentration of hop extracts against microorganisms after 24h incubation. Beige color stands for hydalcoholic-extract, pink for hydroacetonic-extract, blue for CO2-extract.

Table 58: Results of meta-analysis process. The table illustrates MIC value along with Confidence Interval (CI), p-value after meta-analysis of classcompound3 against different strains by class stratification for 48 hours incubation. Finally, it shows the number of studies being used.

class	classcompound3	hours	number of studies	effect	confidence interval	value	df	p-value	I ²
Bacilli	flavonoids	48	19	434,914	126,106-743,723	5,40E+07	18	0	100%
Gammaproteobacteria	flavonoids	48	8	575	130,098-1019,902	1,10E+07	7	0	100%
Bacteroidia	flavonoids	48	7	39,429	27,795-51,062	5918,86	6	0	100%
Clostridia	flavonoids	48	33	55,03	47,712-62,348	58882,88	32	0	99,90%
Actinomycetia	flavonoids	48	2	46,875	16,251-77,499	1464,84	1	0	99,90%
Saccharomycetes	flavonoids	48	3	50	30,4-69,6	2400	2	0	99,90%
Bacteroidia	bitter acids	48	14	512,857	287,914-737,8	9,60E+06	13	0	100%
Clostridia	bitter acids	48	66	424,667	316,665-532,668	5,20E+07	65	0	100%
Saccharomycetes	bitter acids	48	7	571,429	339,269-803,588	2,40E+06	6	0	100%

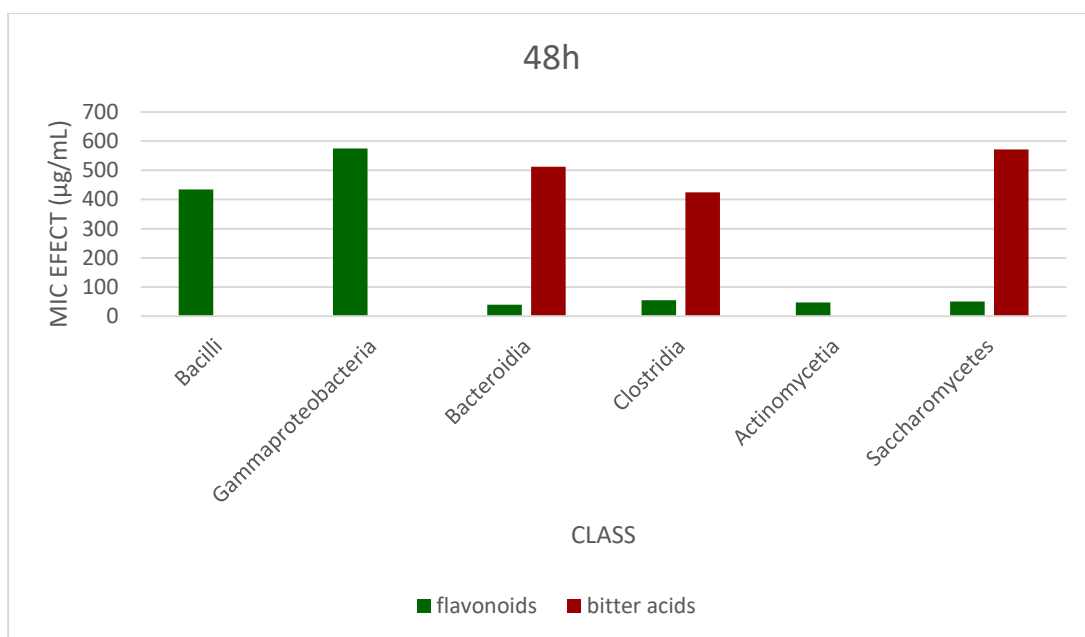


Figure 78: Minimum Inhibitory Concentration of meta-analysis of hop compounds' classes against microorganisms after 48h incubation. Green color stands for flavonoids and dark red for bitter acids.

Table 59: Results of meta-analysis process. The table illustrates MIC value along with Confidence Interval (CI), p-value after meta-analysis of classcompound3 against different strains by class stratification for 48 hours incubation. Finally, it shows the number of studies being used.

class	classcompound3	hours	number of studies	effect	confidence interval	value	df	p-value	I ²
Bacilli	CO2-extract	48	19	32,613	7,247-57,979	2,70E+05	18	0	100%
Gammaproteobacteria	CO2-extract	48	12	2604,167	1550,473-3657,86	1,50E+08	11	0	100%
Actinomycetia	CO2-extract	48	4	15,625	15,059-16,191	0	3	0	100%
Saccharomycetes	CO2-extract	48	4	500	153,524-846,476	1,50E+06	3	0	100%
Actinomycetia	hydralcoholic-extract	48	12	154,667	109,761-199,572	2,10E+05	11	0	100%
Bacilli	hydralcoholic-extract	48	24	86,667	64,579-108,754	2,10E+05	23	0	100%
Fusobacteriia	hydralcoholic-extract	48	12	250,667	154,914-346,419	9,50E+05	11	0	100%
Saccharomycetes	hydralcoholic-extract	48	4	384	239,157-528,843	2,00E+05	3	0	100%
Bacilli	hydroacetic-extract	48	14	92,257	71,858-112,656	4,90E+05	13	0	100%

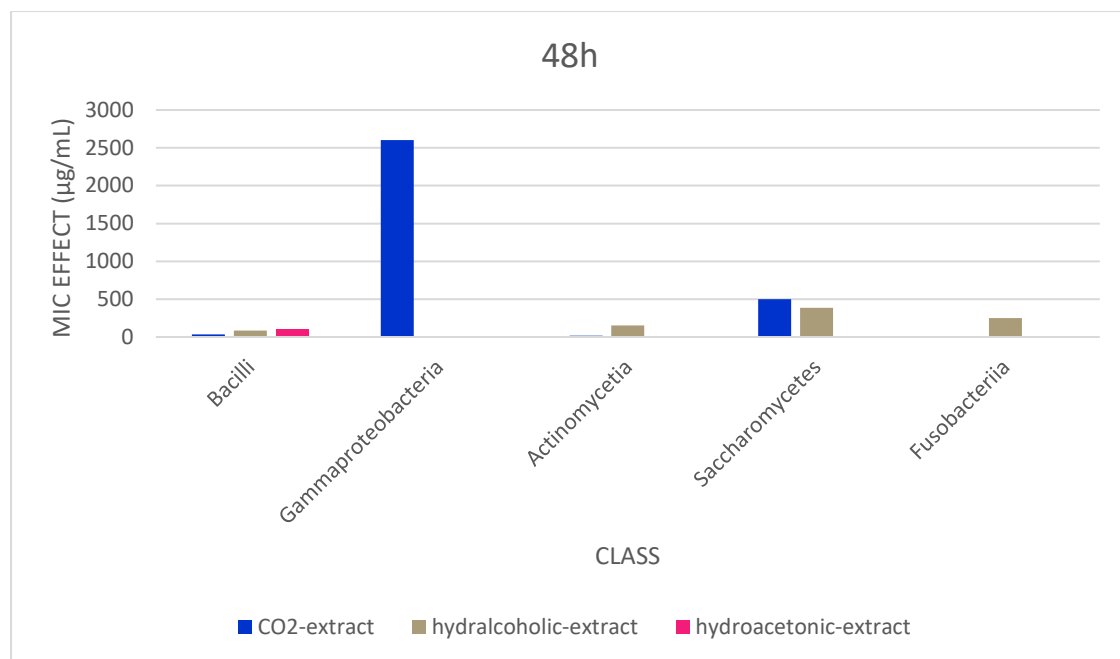


Figure 79: Minimum Inhibitory Concentration of hop extracts against microorganisms after 48h incubation. Beige color stands for hydralcoholic-extract, pink for hydroacetic-extract, blue for CO₂-extract.

