International Journal of Pharmaceutical Drug Design
IJPDD, Vol.-1, Issue-6 (May, 2024)
ISSN: 2584-2897
Website: https://ijpdd.org/

Research

Formulation And Evaluation of microemulsion based Allicin for the treatment of Staph Infection

Rajat Rai*, Dr. M K Gupta, Ankit Yadav, Omkar Singh

Career Point University, National Highway 52, Alaniya, Kota (Rajasthan), India - 325003

Article History
Received: 24/04/2024
Revised : 15/05/2024
Accepted : 24/05/2024

DOI:
10.62896/ijpdd.1.6.11

Abstract:
Micro emulsions have several advantages over emulsions, such as low manufacturing costs, high solubility, good penetrating power, clarity and transparency, the ability to be sterilized through filtration, and thermodynamic stability over an extended length of time. One of the most important components in the creation of a micro emulsion was surfactants. Combining surfactants and co-surfactants can enhance the dispersion of oil in water. The skin acts as an amazing barrier against bacterial infections. Many bacteria touches or reside on the skin, yet most of the time they are unable to create an infection. In the event that bacterial skin infections do develop, they can impact any area of the body, no matter how big or tiny. Depending on how bad they are, they could be harmless or even deadly. Bacterial skin infections can arise when bacteria enter the skin through hair follicles or microscopic skin breaks brought on by burns, sunburns, animal or insect bites, wounds, or pre-existing skin diseases. People are prone to developing bacterial skin illnesses following a variety of activities, such as gardening in contaminated soil or swimming in a contaminated pond, lake, or ocean. Antibiotics used topically are drugs used to treat bacterial infections.

Keywords: *Microemulsions, Skin infections, Bacteria, Antibiotics, Co-surfactants*

***Corresponding Author**
Rajat Rai
Career Point University, National Highway 52, Alaniya, Kota (Rajasthan), India – 325003
Email: rajatrai448@gmail.com

1. Introduction:

When compared to oral and parenteral medication delivery, cutaneous delivery of drugs provides a more appealing and alternate method of drug administration. It gets over the hepatic first-pass metabolism and gets around the issues with oral medication distribution, such as hepatic clearance and GI degradation [1]. It is also a more convenient and non-invasive method of medication administration than the parenteral route, which is why it is chosen [2]. Despite these benefits, there are a number of drawbacks to cutaneous drug administration, such as low drug penetration and reduced bioavailability as a result of the stratum corneum, the skin's protective layer [3]. Since the skin is the body's first line of defence, it views all medications and their excipients as external substances and prevents them from entering the body [4].

Skin medication delivery is significantly hampered by this phenomenon. The dermis, subcutaneous tissues, and epidermis make up the three layers of human skin. The outermost layer of skin, known as the epidermis, is made up of five layers that are arranged from outside to inside: 1) stratum corneum; 2) stratum lucidum; 3) stratum granulosum; 4) stratum spinosum; and 5) stratum germinativum. The keratinocytes that make up this layer are in charge of producing keratin. Collagen fibres make up the middle layer, known as the dermis. It is made up of blood vessels, sweat glands, hair follicles, nerve endings, and sebaceous glands. This layer finishes in the subcutaneous tissues, which are made up of adipose tissues and fat globules [5-8].

In comparison to emulsions, microemulsions have a number of advantages, including thermodynamic stability over a long period of time, clarity and transparency, the capacity to be sterilised through filtration, low manufacturing costs, high solubility, and good penetrating power. Surfactants were one of the most crucial elements in the formation of a microemulsion [9]. The dispersion of oil in water can be improved by using co-surfactants and surfactants in combination. [10]. A remarkable barrier against bacterial infections is provided by the skin. Despite the fact that many bacteria come into touch with or live on the skin, they typically cannot cause an infection [11].

When bacterial skin infections do arise, they can affect any part of the body, whether it be a small patch or the full surface [12]. They may be innocuous or potentially fatal, depending on their severity. When bacteria penetrate the skin through hair follicles or tiny skin breaks caused by scrapes, punctures, surgeries, burns, sunburn, animal or insect bites, wounds, or pre-existing skin conditions, bacterial skin infections can develop [13].

After engaging in a range of activities, such as gardening in polluted soil or swimming in a contaminated pond, lake, or ocean, people are susceptible to contracting bacterial skin diseases [14]. Topical antibiotics are medications used topically to treat bacterial infections. Topical medicines can be administered to the skin with ease and at high concentrations to reach effective levels locally with low systemic harm. High local antibiotic concentrations that can be attained using topical preparations can aid in the eradication of bacteria in bacterial biofilms [15].

Microemulsions, nanoemulsions, nanocapsules, nanovesicles, transferosomes, liposomes, and hydrogel systems are a few examples of the colloidal-based drug delivery systems [19]. Because of its adaptability, biocompatibility, and ability to penetrate a drug molecule to deep layers of skin due to unique hydration properties of microemulsion ingredients as well as the longer shelf life of formulation, the microemulsions-based drug delivery has proven to be a thermodynamically stable and clinically beneficial system [20].

Famous antibacterial, antifungal, antioxidant, antigiardial, and antidiabetic agents include herbal extracts and essential oils. According to reports, several herbal ingredients, including essential oils and oil-based formulations, are effective antibacterial agents that can be utilised to stop food rotting. The potential of oil components to harm bacterial membranes and subsequently cause cell lysis may be the cause of the antibacterial activity [21]. Traditional medical systems all around the world recommend essential oils for a range of health problems. Due of the antibacterial qualities of essential oils, aromatherapy has been utilised to treat significant skin conditions. These activities include antibacterial, antibacterial, anticancer, antimutagenic, antidiabetic, antiviral, and anti-inflammatory properties[22]. Therefore, an effort is made in the current work to examine the synergistic antibacterial effects for treating staph infection and research the effect of allicin to be prepared as microemulsion.

Role of micro emulsions as antibiotic:

The treatment of topical and/or systemic infections in humans and animals is becoming more and more problematic due to the antibiotic resistance of various bacterial strains, which is often exhibited by both Gramme positive and Gramme negative bacteria [1]. In addition, a number of yeast species, most notably those in the genus Candida, are regarded as emerging pathogens in both veterinary and human medicine. Moreover, some of these fungal species exhibit both acquired and innate medication resistance. Drug resistance in dermatophytes has also been documented, however it does not have the same effect as in bacteria.

Over 150 years of natural medicine have been used to treat infectious diseases; currently, botanicals, such as plant extracts and essential oils (EOs), are thought to offer the most sustainable, safe, and effective approach in terms of resistance, safety, and efficacy [3]. These are the reasons why veterinarians and animal owners especially value them. Since ancient times, EOs, in particular, have been recognised as preservatives and anti-infective agents. EOs are combinations of volatile, lipophilic, and low-molecular-weight chemicals, including monoterpenoids, sesquiterpenoids, and phenylpropanoids. They are still employed as preservatives in food, medicine, and cosmetics, in accordance with tradition [4,5]. T

As "thermodynamically stable isotropic liquids formed by mixing oil, water, and surfactants together," microemulsions (MEs) are a sort of nano-dispersion system [20]. Their small dispersion phase size ($r<100$ nm) bestows upon them numerous potential advantages for a variety of applications, including improved long-term stability (thermodynamic stability), increased solubility and consequently bioavailability of active ingredients, uniform dispersion and sustained release, and quick penetration of actives into the target site.

Certain EOs proved to be effective against strains that were both Gram-positive and Gram-negative in this regard. Because EOs are hydrophobic, they can partition on the microbial membrane, upsetting its structure and allowing ions and intracellular organelles to escape [7].

Effects of*Staphylococcus aureus*:

The human immune system's component skin microbiota is made up of a diverse range of living organisms. One of the fundamental elements of the typical flora that lives in the moist squamous epithelium of the anterior nares is *Staphylococcus aureus*. In addition, the skin, throat, perineum, axillae, and vagina are frequently sites of carriage [23]. Twenty to thirty percent of healthy people have a chronic *S. aureus*colonisation, while the remaining people are low-level intermittent carriers. A person may harbour several strains of the bacteria in various anatomical locations at different frequencies, or they may harbour a single strain of the bacteria for a lengthy period of time [24].

Even with these inherent characteristics, *S. aureus* has the potential to be a serious opportunistic human disease. This adaptable microbe can cause a wide range of diseases, from superficial to invasive infections, by infecting different anatomical sites. In fact, the bacterium was discovered in the 1880s from abscesses in a knee joint [25]. As a result, it is now a major contributor to meningitis, bacteremia, osteomyelitis, urinary tract infections, septic arthritis, pneumonia, and toxic shock syndrome. Furthermore, S. aureus is the causative agent of a variety of skin and soft tissue infections (SSTIs), some of which are benign (such as simple cellulitis and impetigo) and others of which are potentially fatal [26].

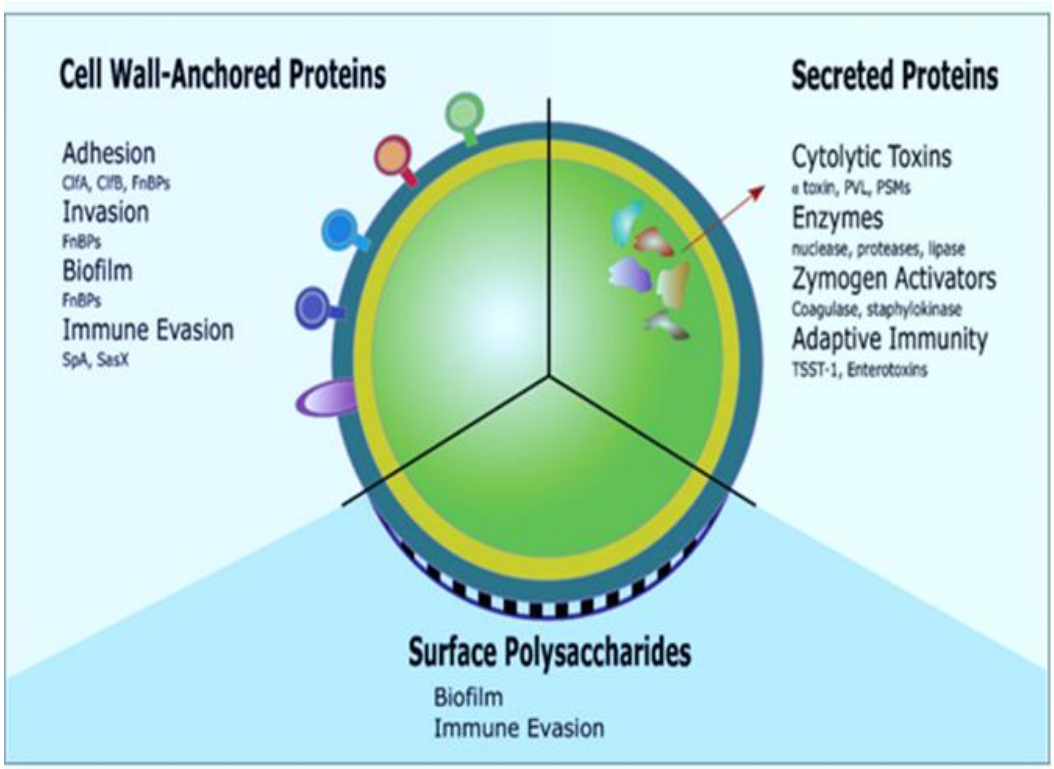

Figure 1: Staphylococcus aureus virulence factors

Effects of herbal compounds on *S. aureus:*

For millennia, people have used herbs in cooking and medicine due to their qualities, which include the presence of numerous biologically active natural chemicals. Herbal combinations have the power to strengthen the nervous, respiratory, digestive, and circulatory systems, prevent disease, renew the body, and control intestinal flora. The study's goal is to present a few key medicinal plant species that are significant to human health [27].

Herbal preparations can be used topically or topically and are made from dried or fresh plants that have been adequately ground up. They generally strengthen the body and aid in maintaining good health. Herbs are utilised in culinary, cosmetic, and fragrance arts in addition to herbal medicine.

The biologically active substances found in herbs, such as glycosides, flavonoids, alkaloids, essential oils, tannins, bitterness, locks, pectin, minerals, and vitamins, give them their valuable, healthful qualities. Herbs when paired properly can be safe, natural remedies for a wide range of ailments. industries [28].

Herbal medicine is a useful tool for maintaining good health through illness prevention and treatment. Herbs can lower blood cholesterol, lower the risk of cancer and cardiovascular disease, and assist the digestive and respiratory systems. They also have antimicrobial qualities. The right choice of herbs and how they are consumed are essential because some of them are hazardous, and using them should not be done when suffering from certain diseases or physiological conditions [29].

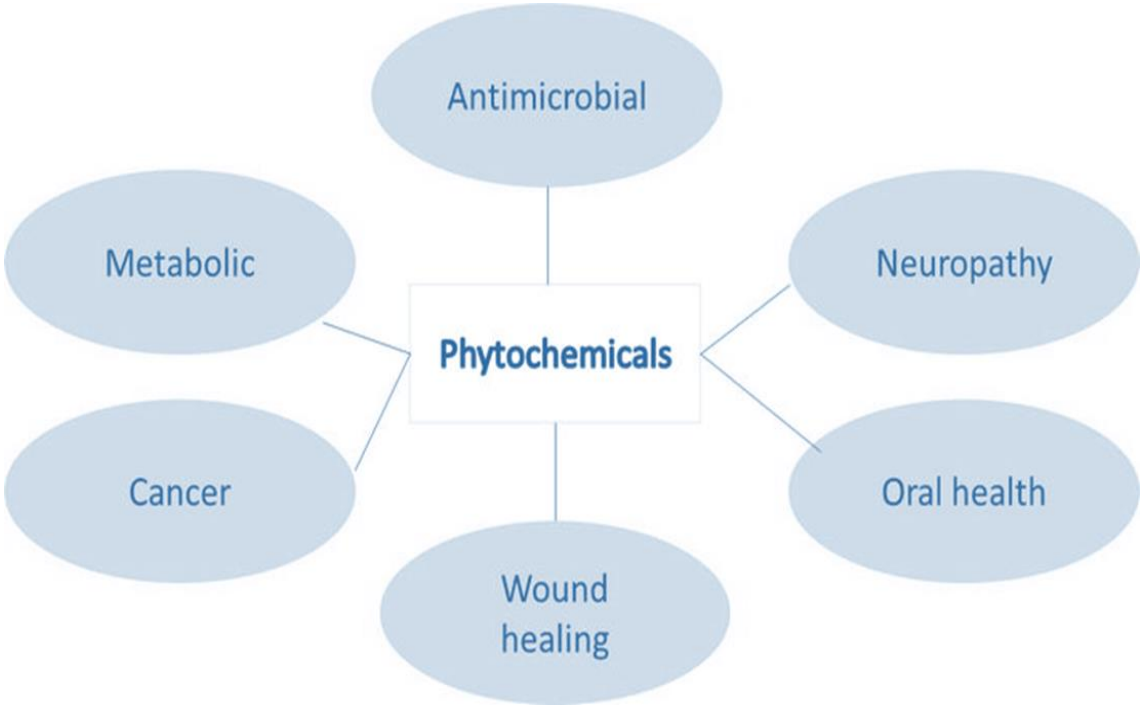

Figure 2: Phytochemicals role for medicinal properties

One bacterium that is thought to be primarily responsible for nosocomial infections is Staphylococcus aureus. Globally, there is a major issue with the rise of antibiotic-resistant S. aureus strains causing infection outbreaks among hospitalised patients. The mecA gene, which encodes PBP 2a, an enzyme (78 kDa) in the bacterial cell wall with a low affinity for b-lactam antibiotics that renders cell wall formation in inactivating quantities of medicines for other PBPs, is present in the majority of clinical MRSA isolates, which were originally identified approximately 40 years ago.This has been linked to colonisations acquired in hospitals, as well as a notable rise in the number of deaths and infections in nosocomial settings. Essential oils and plant extracts have long been used for many purposes. Investigations on the antibacterial, antifungal, antiviral, insecticidal, anticancer, and other properties of essential oils of herbal compounds [30].

Phytochemicals showing medicinal properties:

Plants create phytochemicals, which are bioactive molecules derived from plants, to defend themselves. There are many different sources of phytochemicals, including whole grains, fruits, vegetables, nuts, and herbs. To date, over a thousand phytochemicals have been identified. Carotenoids, polyphenols, isoprenoids, phytosterols, saponins, dietary fibres, and certain polysaccharides are a few of the important phytochemicals. In additon to having potent antioxidant properties, these phytochemicals have antiviral, antibacterial, antidiarrheal, anthelmintic, and antiallergic properties. In addition, they support immunity, promote gap junction communication, control gene transcription, and

guard against prostate and lung malignancies. The features of functional foods have been expanded by the new emphasis on translational research [31].

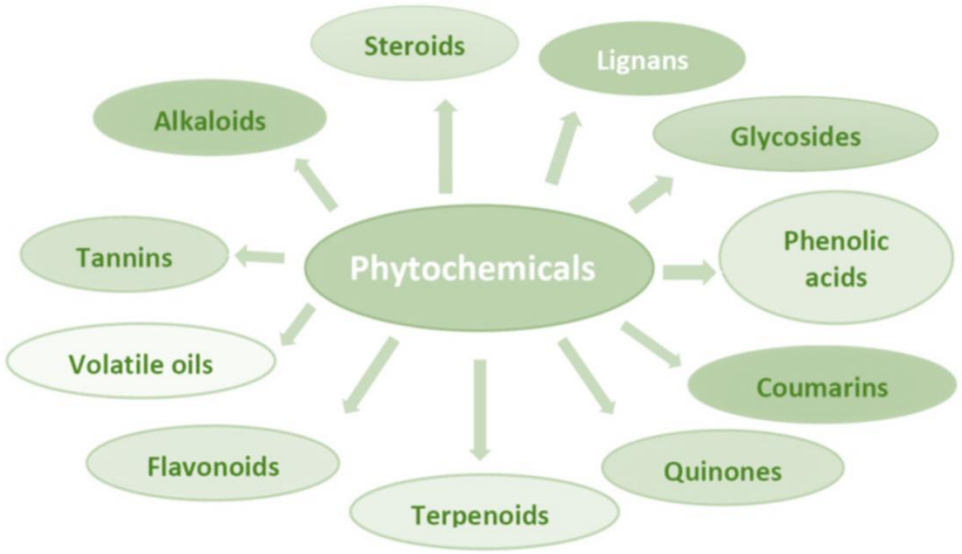

Figure 3: Types of phytochemicals for antimicrobial properties

Allicin as antibiotic:

One of the active ingredients in freshly crushed garlic homogenates, allicin, possesses a range of antibacterial properties. Pure allicin was found to have the following properties: i) antibacterial activity against a broad spectrum of Gram-positive and Gram-negative bacteria, including multidrug-resistant enterotoxicogenic strains of Escherichia coli; ii) antifungal activity, especially against Candida albicans; iii) antiparasitic activity, including against some major human intestinal protozoan parasites like Giardia lamblia and Entamoeba histolytica; and iv) antiviral activity. Allicin's primary antimicrobial activity stems from its chemical interaction with thiol groups of several enzymes, such as RNA polymerase, alcohol dehydrogenase, and thioredoxin reductase. These interactions can impact the vital metabolism of cysteine proteinase activity, which is linked to the pathogenicity of Escherichia coli [32].

References:

1. N. Cassir, J. Rolain, P. Brouqui, A new strategy to fight antimicrobial resistance : the revival of old antibiotics, Front. Microbiol. 5 (2014) 1–15.
2. N.M. Martinez-Rossi, T.A. Bitencourt, N.T.A. Peres, E.A.S. Lang, Dermatophyte resistance to antifungal Drugs : mechanisms and prospectus, Front. Microbiol. 9 (2018) 1–18.
3. R. Pavela, G. Benelli, Essential oils as ecofriendly Biopesticides ? Challenges and constraints, Trends Plant Sci. 21 (2016) 1000–1007, https://doi.org/10.1016/j. tplants.2016.10.005.
4. N. Leyva-Lopez, E.P. Guti, G. Vazquez-olivo, J.B. Heredia, Essential oils of Oregano : biological activity beyond their antimicrobial properties, Molecules 22 (2017) 989.
5. L. Kokoska, P. Kloucek, O. Leuner, P. Novy, Plant-derived products as antibacterial and antifungal agents in human health care, Curr. Med. Chem. (2018).
6. G. Lang, G. Buchbauer, A review on recent research results (2008 – 2010) on essential oils as antimicrobials and antifungals . A review, Flavour Fragrance J. 27 (2012) 13–39.
7. M.G. Miranda-novales, F. Solo, Essential oils from aromatic herbs as antimicrobial agents, Curr. Opin. Biotechnol. 23 (2012) 136–141.
8. M. Isman, Pesticides based on plant essential oils : from traditional practice to commercialization, Nat. Occur. Bioact. Compd. (2006) 29–44.
9. R. Pavela, G. Benelli, L. Pavoni, G. Bonacucina, M. Cespi, K. Cianfaglione, I. Bajalan, M. Reza, G. Lupidi, D. Romano, A. Canale, F. Maggi, Industrial Crops & Products Microemulsions for delivery of

Apiaceae essential oils — towards highly effective and eco-friendly mosquito larvicides ? Ind. Crops Prod. 129 (2019) 631–640.

10. S. Paul, R.C. Dubey, D.K. Maheswari, S. Chul, Trachyspermumammi(L .) fruit essential oil in fluencing on membrane permeability and surface characteristics in inhibiting food-borne pathogens, Food Control 22 (2011) 725–731, https://doi.org/ 10.1016/j.foodcont.2010.11.003.
11. R. Iannarelli, O. Marinelli, M. Beatrice, G. Santoni, C. Amantini, M. Nabissi, F. Maggi, Industrial Crops & Products Aniseed (Pimpinellaanisum L .) essential oil reduces pro-in flammatory cytokines and stimulates mucus secretion in primary airway bronchial and tracheal epithelial cell lines, Ind. Crops Prod. 114 (2018) 81–86.
12. F.A. Al-bayati, Synergistic antibacterial activity between Thymus vulgaris and Pimpinella anisum essential oils and methanol extracts, J. Ethnopharmacol. 116 (2008) 403–406.
13. Kosalec, Antifungal activity of fluid extract and essential oil from anise fruits (Pimpinellaanisum L ., Apiaceae), Acta Pharm. 55 (2005) 377–385.
14. E. Carrió, J. Vallès, Ethnobotany of medicinal plants used in eastern mallorca (balearic islands, mediterranean sea), J. Ethnopharmacol. 141 (2012) 1021–1040.
15. R. Pavela, F. Maggi, G. Lupidi, K. Cianfaglione, X. Dauvergne, M. Bruno, G. Benelli, Efficacy of sea fennel (Crithmummaritimum L., Apiaceae) essential oils against Culex quinquefasciatus Say and Spodoptera littoralis (Boisd.), Ind. Crops Prod. 109 (2017) 603–610.
16. G. Ruberto, M.T. Baratta, S.G. Deans, H.J.D. Dorman, Antioxidant and antimicrobial activity of foeniculum vulgare and Crithmummaritimum essential oils, Planta Med. (2000) 687–693.
17. F. Senatore, F. Napolitano, M. Ozcan, F. Ii, V.D. Montesano, I. Napoli, S. Naturali, F. Ii, V.D. Montesano, I. Napoli, Composition and antibacterial activity of the essential oil from CrithmummaritimumL .(Apiaceae) growing wild in Turkey, Flavour Fragrance J. 15 (2000) 186–189.
18. A.R. Bilia, C. Guccione, B. Isacchi, C. Righeschi, F. Firenzuoli, M.C. Bergonzi, Essential oils loaded in Nanosystems : a developing strategy for a successful therapeutic approach, evidence-based complement, Altern. Med. 2014 (2014).
19. D.J. Mcclements, Nanoemulsions versus microemulsions : terminology , differences , and similarities, Soft Matter 8 (2012) 1719–1729.
20. M.R. Patel, R.B. Patel, J. Parikh, K.K. Bhatt, A. Solanki, Investigating the effect of vehicle on in vitro skin permeation of ketoconazole applied in O/W microemulsions, Acta Pharm. Sci. 52 (2010).
21. G.N. El-hadidy, H.K. Ibrahim, M.I. Mohamed, M.F. El-milligi, Microemulsions as vehicles for topical administration of voriconazole : formulation and in vitro evaluation, Drug Dev. Ind. Pharm. 38 (2012) 64–72.
22. F.M. Hashem, D.S. Shaker, M.K. Ghorab, M. Nasr, A. Ismail, Formulation , characterization , and clinical evaluation of microemulsion containing clotrimazole for topical delivery research article formulation , characterization , and clinical evaluation of microemulsion containing clotrimazole for topical delivery, AAPS PharmSciTech 12 (2011) 879–886.
23. L. Kumar, S. Verma, A. Bhardwaj, S. Vaidya, B. Vaidya, Eradication of superficial fungal infections by conventional and novel approaches: a comprehensive review, Artif. Cells, Nanomedicine, Biotechnol. 42 (2014) 32–46.
24. M. Kreilgaard, I nfluence of microemulsions on cutaneous drug delivery, Adv. Drug Deliv. Rev. 54 (2002) S77–S98.
25. R.R. Shah, C.S. Magdum, K.A. Wadkar, N.S. Naikwade, Fluconazole topical microemulsion: preparation and evaluation, Res. J. Pharm. Technol. 2 (2009) 353–357.
26. R. Pavela, L. Pavoni, G. Bonacucina, M. Cespi, N.G. Kavallieratos, L. Cappellacci, R. Petrelli, F. Maggi, G. Benelli, Rationale for developing novel mosquito larvicides based on isofuranodiene microemulsions, J. Pest Sci. 92 (2019) (2004) 909–921.

27. H. Zhang, Y. Shen, P. Weng, G. Zhao, F. Feng, X. Zheng, International Journal of Food Microbiology Antimicrobial activity of a food-grade fully dilutable microemulsion against Escherichia coli and Staphylococcus aureus, Int. J. Food Microbiol. 135 (2009) 211–215.
28. H. Zhang, Y. Xu, L. Wu, X. Zheng, Anti-yeast activity of a food-grade dilution-stable microemulsion, Appl. Microbiol. Biotechnol. 87 (2010) 1101–1108.
29. I.S.I. Al-adham, H. Ashour, E. Al-kaissi, E. Khalil, M. Kierans, P.J. Collier, Studies on the kinetics of killing and the proposed mechanism of action of microemulsions against fungi, Int. J. Pharm. 454 (2013) 226–232.
30. G. Bonacucina, M. Cespi, M. Misici-falzi, G.F. Palmieri, Colloidal soft matter as drug delivery system, J. Pharm. Sci. 98 (2009) 1–42.
31. G. Benelli, R. Pavela, R. Iannarelli, R. Petrelli, L. Cappellacci, K. Cianfaglione, F. Heshmati, M. Nicoletti, A. Canale, F. Maggi, Synergized mixtures of Apiaceae essential oils and related plant-borne compounds : larvicidal effectiveness on the filariasis vector Culex quinquefasciatus Say, Ind. Crops Prod. 96 (2017) 186–195.
32. S. Balasubramani, T. Rajendhiran, A.K. Moola, R. Kumari, B. Diana, Development of nanoemulsion from Vitex negundo L . essential oil and their efficacy of antioxidant , antimicrobial and larvicidal activities (Aedes aegypti L .), Environ. Sci. Pollut. Res. 24 (2017) 15125–15133,

*****