International Journal of Chemistry and Pharmaceutical Sciences

ISSN: 2321-3132 | CODEN (USA): IJCPNH

Available online at:http://www.pharmaresearchlibrary.com/ijcps

Research Article

Synthesis and Extraction of Eugenol

Medisetty Kavya*, G Sujatha

Ratnam Institute of Pharmacy, Pidthapolur (V), Muthukur (M), Nellore (Dt), Andhra Pradesh–524343, India.

Abstract

Eugenol, a phytogenic bioactive component is frequently found in diversified herbal plants possessing well-defined functional attributes. Prominent sources of eugenol are clove, cinnamon, Tulasi and pepper. Various extraction methods have been practiced globally for the extraction of eugenol and other nutraceutics from plants. The most extensively employed approaches in this regard include solvent extraction, hydrodistillation, microwave-assisted extraction, supercritical carbon dioxide extraction and ultrasound-based extraction. Eugenol has been approved to encompass numerous beneficial aspects against a capacious spectrum of lifethreatening indispositions including oxidative stress, inflammation, hyperglycemia, elevated cholesterol level, neural disorders and cancer. In addition, eugenol has also shown strong potential as an antimicrobial agent against wide ranges of pathogenic and spoilage causing microorganisms. Predominantly, the principle mechanistic approaches associated with the therapeutic potential of eugenol include its free radical scavenging activity, hindrance of reactive oxygen species' generation, preventing the production of reactive nitrogen species, enhancement of cyto-antioxidant potential and disruption of microbial DNA & proteins. Consequently, this article is an attempt to elucidate the general properties, sources, extraction methods, therapeutic role and associated mechanisms of eugenol.

Keywords: Eugenol, Thinlayer chromatography, high performance thin layer chromatography, extraction.

Article History: Received 10 Aug 2023, **Accepted** 11 Sept 2023, **Available Online** 17 Oct 2023

Citation: Medisetty Kavya, *et al. Synthesis and Extraction of Eugenol, Int. J. of Chem. and Pharm. Sci., 11(1), 2023: 49-54.*

Contents:

***Corresponding author**
Medisetty Kavya,
Ratnam Institute of Pharmacy,
Pidthapolur (V), Muthukur (M),
Nellore (Dt), Andhra Pradesh – 524343, India.

JOURNAL QR-CODE

1. Introduction

It is no secret today that plastic materials surround us, helping us with housing, personal care, packaging, clothing, transport, or electronics in everyday life without attracting attention; but when we are done using these plastic materials, they turn out to be very "visible", that is, problematic. The great majority of plastics, which are prepared from petroleum-derived chemicals, are not biodegradable materials and thus usually pile up as waste in the environment if not recovered and reused. Containing toxic volatile organic components, plastics represent the most significant and dangerous pollutants to human health and the environment. To satisfy our demands and needs, numerous types of specific plastics were created and are still constantly developed. Among this variety of polymers, epoxy resins (thermosetting polymers) used in composites for manufactured products stand out as useful materials with exceptional mechanical, adhesive, heathier.

Epoxy resin was discovered in 1909 by Russian organic chemist Nikolai A. Prilezhaev acid catalysis furnishing epoxides, also called oxiranes. 1–3 Much later, in the 1940s and (Prileschajew) when he developed an olefin epoxidation reaction under perbenzoic 1950s, chemists in the United States and Switzerland introduced the first epoxy derivatives that are now known as low-molecular weight prepolymers based on a 4,4-isopropylidene diphenol structure (bisphenol A, BPA), which is also employed for the production of polycarbonate. Today, the manufacture of polycarbonates and epoxy resins represents approximately 68% and 30% of the production capacity of BPA, respectively. These materials are used extensively in the manufacture of adhesives, plastics, paints, and numerous commercial products.4 However, numerous studies on very-low-dose exposure to BPA 1 (Figure 1a) indicate that this compound, whose annual production is over 4.5 million tons, exhibits adverse health effects, including breast and prostate cancer, obesity, neurobehavioral problems, and reproductive abnormalities.

Its main secondary effects are associated with estrogen-like activity acting as a potential endocrine disruptor.6,7 Thus, some countries have enacted laws to ban BPA usage for the manufacture of infant bottles or printing ink. Its derivative, diglycidyl ether (DGEBA) 2 (in oligomeric form 3) (Figure 1a), has excellent properties and is currently the most widespread epoxy monomer. Nevertheless, due to close structural similarity to BPA, DGEBA-based materials could have the same negative pharmacological profile. In addition to these serious toxicity problems, BPA and its derivatives are petroleum based phenols, that is, their fossil resources will eventually be subject to increasing scarcity and prices. Thus, due to the rapid depletion of petroleum reserves, global warming, and other environmental problems, there is growing interest in the utilization of large biobased feed stocks in both academic and industrial laboratories. Modern biorefining processes operate numerous feedstock streams, such as carbohydrates, tanninoids, terpenoids, lignin, and vegetable or essential oils; all of these could be used to create novel platform chemicals with structural features that are not readily available from traditional petrochemical refining processes. In the context of new BPA/DGEBA replacements with both enhanced performance and reduced toxicity and the development of innovative biobased polymers and thermosetting resins, the conversion of plant biomass into useful polymeric materials is believed to have considerable environmental and economic value. Showing reduced toxicity and reduced production costs, some bioderived materials look very attractive as sustainable alternative precursors for the preparation of monomers and polymers.9–12 Among them, natural phenols, such as lignocellulosic derivatives (i.e., vanillin (4),13–15 ferulic acid (5),16 and guaiacol (6) 17), the 3-alkenyl phenolic molecule cardanol (7), 18– 20 anethole (8),21 or (iso) eugenols (9–10), the main monolignol constituents of clove oil 22 and other similar phenolic molecules (Figure 1b) are all being considered as sustainable alternatives and potential molecular replacements for BPA and DGEBA in epoxy resin 11 manufacturing.

Among these green platform base chemicals, (iso) eugenols are gaining increasing interest, not only due to their sourcing but also due to their structure and chemical properties that could enhance the physical characteristics of thermosetting epoxy materials. For example, clove bud essential oil from the trees Syzygiumaromaticum and Eugenia caryophyllata, has eugenol (2- methoxy-4-[2-propenyl] phenol), which constitutes 60%–90% of distilled clove bud oil,23 as its key component. Clove bud essential oil is one of the most important biobased chemicals, with an estimated annual production of 80 000 tons, and it is used as a flavoring substance and as an antimicrobial and antiseptic additive in fragrances and cosmetics, with prices ranging from ~$12/kg (clove leaf oil) to ~ $80/kg (clove bud oil) in 2016. Although natural clove-based eugenol represents a limited resource, there are potential chemical methods for its production. For example, the depolymerization of lignin is a very promising strategy for the production of eugenol. Other lignocellulosic derivatives 4,5 and naturally occurring guaiacol (6) obtained from softwood Kraft lignin could also be used for developing cleaner eugenol-based products and processes.

Fig 1: Molecular structures of BPA, DGEBA and selected natural phenols as alternative replacements

On the other hand, current chemical processes follow a linear path in which a substantial amount of raw material is lost at every step as waste or emissions.30 Therefore, industrial chemistry needs to refresh itself as a promoter of sustainable development for delivering practical, realistic, and efficacious solutions through original workup, repair, remanufacture, upgrades, and retrofits.31 In this context, a future transition period from linear to circular chemistry should promote a switch from the utilization of fossil reserves to renewable or "green" resources, that is, lignocellulosic feedstock, in future biorefineries, minimizing nonrenewable resource consumption and waste and using waste as a secondary resource for improving industrial ecosystems. The twelve guiding principles of green chemistry are crucial to achieving the five R (R5) concept (Reduce, Reuse, Repurposing, Recycling, and Recovery) for the development of circular organic chemistry. This transition to the circular process requires the sustainable production of chemicals using crude renewable resources via combined biological and chemical conversion routes. Within this framework and the timely formulation of twelve principles for circular chemistry, natural phenolic chemicals such as eugenol and/or their combinations could offer circularity in the chemical industry of epoxy them stable thermoplastic polymers and related polymeric materials (Figure 2).

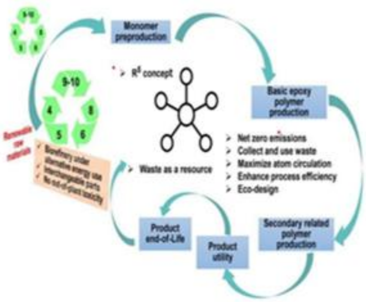

Fig 2: A methodological framework to analyze the development of a circular eugenol-monomer chemistry processor for epoxy thermo stable polymer production using the concepts of green chemistry and circular chemistry.

2. Extraction Methods

Steam Distillation:

The most common method for the isolation of eugenol is steam distillation. In the extraction and isolation process of eugenol, firstly essential oil is extracted from the plants. Afterwards, the essential oils are mixed with 3% solution of sodium or potassium hydroxide for the extraction of eugenol. This reaction results in the formation of a phenolic alkali salt. The insoluble portion of the extract is then isolated by solvent extraction or steam distillation. The remaining alkaline solution is then acidified at refrigeration temperature followed by the liberation of eugenol by employing various techniques such as fractional distillation, high pressure liquid chromatography (HPLC) or thin layer chromatography (TLC). At the end obtained eugenol is verified by employing modern spectroscopic techniques like Fourier transform infrared spectroscopy (FTIR), Fourier transform near infrared spectroscopy (FTNIR), mass spectroscopy (MS) and nuclear magnetic resonance (NMR). Some important methods for the extraction of eugenol from various plant sources are described herein.

Clove (Syzygiumaromaticum), one of Indonesian native species, is an aromatic flower buds. Java and Manado are parts of the largest clove productions in Indonesia. Beside used as cooking ingredients directly, clove can be proceed furthermore as medicinal properties. As medicinal effect, clove buds need to undergo the extraction process to obtain the essential oil.

Solvent extraction

Solvent extraction is one of the most common and extensively employed methods for the extraction of essential oils from plants. Accordingly, eugenol has also been extracted using various solvents like methanol, ethanol, petroleum ether and N hexane. The major hindrances of solvent extraction are inclusion of other soluble residues undesirable flavor changes in the food. However, still this method has wide applications for the extraction of eugenol and other essential oils from various aromatic herbs. In a typical solvent extraction process of eugenol from clove, the clove buds are ground and wrapped in filter paper followed by subjecting the filter paper to the extraction thimble and inserting into the reflux flask having 500 mL capacity. Afterwards, extraction is carried out by using a suitable organic solvent in Soxhlet apparatus. The process ends by concentrating the obtained extracts at 50 C using rotary vacuum evaporator. Several modifications have been made in the conventional solvent extraction process, which show higher efficiency as compared to the traditional method. As an instance, batch extraction process is an attractive alternative to the Soxhlet extraction. This method employs the use of reactor equipped with agitator having four blades and motor having 1200 rpm speed. Recently, this method was studied by Garkal et al. who extracted eugenol from leaves of tulsi plant using methanol as solvent and reported satisfactory extraction efficiency. They further reported that extraction efficiency of eugenol was not affected by agitation speed.

Hydro distillation:

Hydro-distillation is also one of the mostly used methods for the extraction of essential oils.9 During hydro distillation method, powdered sample (100 g dried and ground clove buds) is soaked into water. To carry out hydro-distillation, dried clove sample is taken into 500 mL volumetric flask and subjected to hydro-distillation for 4–6 hours. Subsequently, the volatile distillate is collected and saturated with sodium chloride following the addition of petroleum ether or other suitable organic solvent. Later, hydro and ether layers are separated and dehydrated by using anhydrous sodium sulphate. Eventually, the sample is heated in water bath at 60 °C for the recovery of ether and concentration of extract. The average yield of oil using hydrodistillation is about 11.5% whereas reported eugenol concentration is 50.5– 53.5%. However, extraction yield can be increased by reducing the particle size of ground clove buds.

Microwave assisted extraction

Traditional methods practiced for the extraction of eugenol from various plant sources are associated with several drawbacks like hydrolysis, thermal degradation and leaching of some fragrance components. To combat these problems, several modern extraction methods have been introduced which provide high extraction yield along with reduced processing time and energy demands. Among these approaches microwave assisted extraction (MWAE) is regarded as a green extraction approach having ability to produce eugenol and other essential oils with same sensorial attributes and quality as those attained by conventional methods. This technique also provides rapid extraction rate at lower cost as compared to the traditional methods. Several configurations have been developed using microwave extraction process. These techniques include microwave-assisted hydro-distillation (MWHD), coaxial microwave-assisted hydro-distillation (coaxial MWHD), microwave assisted hydro diffusion and gravity (MWHG) and microwave steam distillation (MWSD). Amongst these green extraction approaches, coaxial MWHD extraction is reported to be advantageous with high savings in heating time (400%) and energy demands (30%). Besides, this method is safe, cost effective and has easy scale-up configuration as compared to the other microwave extraction techniques.

Procedure

Method Development The microwave extraction method development was done by undergraduate students as part of a summer research project. Initially optimal solvent composition was determined by varying the water-to-ethanol ratio, as well as testing pure dichloromethane. As summarized below in Table 1, the 50/50 ethanol/water mix worked best for this application. It not only produced better yields compared to theother solvent mixes, but it also produced a better yield than the steam distillation method, i.e an average of 12.6 ± 0.1% versus 10.1% for steam distillation. This solvent mix had the added benefit of extracting only the eugenol, thereby eliminating the need for a subsequent acid-base extraction to isolate it from the acetyleugenol, as would have been needed if the sample were obtained by steam distillation. The liquid-liquid extraction required for the isolation of eugenol can be completed using dichoromethane or n-pentane. Yields are better with dichloromethane, but since n-pentane is a safer solvent and the amounts isolated are enough for IR characterization, we suggest it as a viable alternative.

3. Synthesis

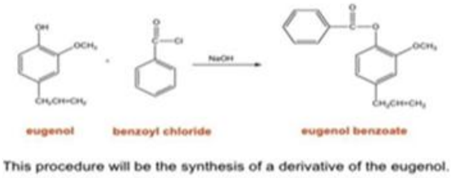

Fig 3: Synthesis of eugenol benzoate

Antioxidant activity

Many human related disorders like cancer, diabetes, arthritis, Parkinson's disease, AIDS and Alzheimer's complications are prompted and exaggerated due to redundant group of the free radicals. Reports have indicated that fruits and vegetables containing cache of phytonutrients like polyphenols, flavonoids and anthocyanin are observed to be efficacious in scavenging the free radicals. Eugenol, a potent phenolic component in clove oil is chiefly responsible for its antioxidant and free radical scavenging activity. Antioxidant power of eugenol can be elucidated by forming complexes with reduced metals. Potent inhibitory effect on lipid peroxidation by isoeugenol and eugenol is administrated to be due to eradication of free radical and formation of iron–oxygenchelate complex, by keeping iron and copper at a reduced state respectively.

Antimicrobial activity

Microbial food-borne illness is currently one of the foremost concerns for food safety authorities, food processing industry and ultimately the consumers. Simultaneously, consumers are concerned regarding the safety aspects of synthetic and artificial food preservatives. Dissemination of methicillin resistant Staphylococcus aureus (MRSA) one of the antibiotic resistant pathogen has provoked researchers to revive the quest for anti-microbial complexes from natural plant sources. Since ancient times, herbs and spices are supplemented in food system, not only to enhance flavoring profile, but also as food preservative and folk medicine. Due to their diversified biological and biochemical functions, plant phytogenic compounds have established a great deal of attention, over past few decades.

Anti-inflammatory activity

Inflammation is known as adaptive immunity response of body that is stimulated by noxious stimuli and other various conditions, for instance tissue injury and infection. It could either be classified as acute or chronic inflammation. Acute inflammation also known to be physiological inflammation is a valuable and constructive host response against tissue damage, but if in time remediation is delayed, it leads to metabolic-associated syndromes as cancer, inflammatory bowel disease (IBD) and rheumatoid arthritis. It is an initial response that results in movement of macrophages and neutrophils from blood stream into infected tissues. Alternatively, chronic inflammation is related to tissue malfunctioning mainly due to persistent exposure to noxious stimuli that results in changes allied with the development of cancer through attraction of bioactive lipids such as eicosanoids, soluble proinflammatory mediators TNF-α and transcription activation factors NF-κB. In the last decade, nutraceutical prospects of eugenol and its derivatives have been exploited by scientists to formulate novel drugs from plant origin having low drug toxicity, mainly those implicating anti-inflammatory potential, to be used in treatment of various maladies.

Therapeutic uses

Eugenol is used as Local Antiseptic and Anesthetic. The wide range of eugenol activities includes Antimicrobial, Anti-inflammatory, Analgesic and Antioxidant. It is often utilized to provide relief from Toothache and Pulpities. This results in the extraction of eugenol from the clove buds by using extraction methods with the help of TLC, HPLC etc.

4. Conclusion

Extraction of essential oils from dried clove leaf by using Solvent-free microwave extraction (SFME) shows that the yield increases with extraction time dan microwave power. The experimental design proves that optimal results can be obtained on certain variables. Extraction experiment results showed that the optimum conditions at 542,037 W microwave power, F / D ratio 0.07 g / mL, extraction time 44.5 minutes. From this optimal condition, the predicted maximum yield is 4.45%. It can be concluded that these results indicate the suitability of the model used in the extraction of essential oils from dried clove leaves (R2 = 0.8906). From GC-MS result, as the chemical analysis shows that essential oils contain a high content of Eugenol, which is 95.68%, in appropriate to the essential oil criteria which have a minimum Eugenol content of 78% (SNI 06-2387-2006). The result of physical properties analysis has a specific gravity of oil that is 1,062 g / mL and cloves leaf oil solubility of 1: 2, it can be concluded that the extraction of clove oil using SFME method has a value in the range of quality requirements to SNI 06-2387-2006 quality standards.

Acknowledgement

The author would like to thank the many students in drug chemistry at Ratnam Institute of Pharmacy Nellore.The structure of these experiments was refines over numerous iterations in various laboratory sections.

5. References

[1] A.Abdou, A.El Amrani, A.Elmakssoudi et.al. Recent advances in Chemical reactivity and Biological activities of eugenol derivatives. Medicinal Chemistry Research. 2021; 30(3):1011-1030.

[2] Beata Olas, Magladalena Ulanowska Biological properties and prospects for the application of eugenol. International journal of Molecular Sciences. 2021;22(3671):1- 13.

[3] D.Chatterjee , P. Bhattacharjee, Supercritical carbon dioxide extraction of eugenol from clove buds, Food Bioprocess Technol., 2013; 23(45):2587–2599.

[4] D. J. Garkal, S. V. Taralkar, P. Kulkarni, et.al. Kinetic model for extraction of eugenol from leaves of Ocimum sanctum Linn (Tulsi), Int. J. Pharm. Appl., 2012; 3(56):267–270.

[5] E.Reverchon C.Marrone, Supercritical extraction of clove bud essential oil: isolation and mathematical modeling, Chem. Eng. Sci., 1997; 20(170): 3421–3428.

[6] E. Schmidt Production of essential oils, in Handbook of Essential Oils: Science, Technology, and Applications, ed. K. H. C. Baser and G. Buchbauer, CRC Press, Taylor and Francis Group, Boca Raton, FL, New York, NY, 2010;456(56): 83–90.

[7] F. Chemat, M. E. Lucchesi, J. Smadja, et.al. Microwave accelerated steam distillation of essential oil from lavender: a rapid, clean and environmentally friendly approach, Anal. Chim. Acta, 2006; 555(678):157–160.

[8] G. P. Kamatou, I. Vermaak A. M. Viljoen, et.al. Eugenol from the remote Maluku Islands to the international market place: a review of a remarkable and versatile molecule, Molecules, 2012; 17(890):6953–6981.

[9] G. Wenqiang, L.Shufen, Y.Ruixiang, et.al. Comparison of essential oils of clove buds extracted with supercritical carbon dioxide and other three traditional extraction methods, Food Chem., 2007;65(56) : 1558–1564.

[10] JamesV. Defrancesco, PhD. Extraction and Analysis of eugenol from cloves. Journal Forensic Science Education .2021;3[2]:1-9.

[11] J.Gonzalez-Rivera, C.Duce, D.Falconieri et.al. Coaxial microwave assisted hydrodistillation of essential oils from five different herbs (lavender, rosemary, sage, fennel seeds and clove buds): chemical composition and thermal analysis, Innovative Food Sci. Emerging Technol., 2010;34(89):308–318.

[12] K.Mostafa, Y.Yadollah, Comparison of essential oil composition of Carum copticum obtained by supercritical carbon dioxide extraction and hydrodistillation methods, Food Chem., 2004;45(76) : 587–591.

[13] Leonor Y.Vargas Mendez, Vladimir V Kouznetsov et.al. Synthesis of eugenol-based monomers for sustainable epoxy thermoplastic polymers. Journal of applied polymer sciences WILEY. 2022; 139 [52237]:2-34.

[14] L.Quan, S.F.Li,S.J. Determination of organochlorine pesticides residue in Ginseng root by orthogonal array design Soxhlet extraction and gas chromatography, Chromatographia, 2004; 34(6): 89–93.

[15] Masnah Banu kamal, Raghavendra Sakirolla Sunday Buru Ayuba et.al. Acomprehensive Review on Eugenols Antimicrobial properties and Industry Applications: A Transformation from Ethnomedicine to Industry. Jurnalfarmasi of ondonesia. 2019; 22[3671]:1-13.

[16] MA Takaeva, R A Bisergaeva, YN Sirieva et.al. Extraction of eugenol, a natural product, and the preparation of eugenol benzoate. Journal of Physics: Conference series.2021;1889, 1-6.

[17] M.A.Vian, X. Fernandez, F.Visinoni et.al. Microwave hydrodiffusion and gravity, a new technique for extraction of essential oils, J. Chromatogr. A, 2008;436(8): 14–17.
[18] MK.Yadav, S.W. Chae, G. J. Im, J.W.Chung ,J.J.Song,et.al.Eugenol: a phytocompound effective against methicillin-resistant and methicillinsensitive Staphylococcus aureus clinical strain biofilms, PLoS One, 2015;43(76) 1-4.
[19] M. R.C. Raja, V. Srinivasan, S. Selvaraj, Versatile and synergistic potential of eugenol: a review, Pharm. Anal. Acta, 2015, 56(6):67-75.
[20] M.T. Golmakani K.Rezaei, Comparison of microwave-assisted hydrodistillation with the traditional hydrodistillation method in the extraction of essential oils from Thymus vulgaris L., Food Chem., 2008; 45(76) 925–930.
[21] N.Gopalakrishnan, P.P.V.Shanti and C.S.Narayanan, Composition of clove (Syzygiumaromaticum) bud oil extracted using carbon dioxide, J. Sci. Food Agric., 2016;67(8);45-52.