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Essential Oils as Alternative *Halal* Therapeutic Source for Lung Cancer: A Mini Review

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Abstract

The global Muslim population is predicted to grow significantly. The market for *Halal* products, an obligation for Muslims, is expanding in sync with the Muslim population. Cancer is a notable cause of death globally. Pharmaceuticals are the most important fundamental component because they are disease-specific, most notably cancer-specific. Optional pharmaceuticals were looked into to meet Muslim demand for *Halal* products. Some essential oils are viable therapeutic sources because they have long been used in conventional medicine for various treatments. The purpose of this study is to review the investigation done on the potential for essential oils to be used as a *Halal* alternative therapy for lung cancer. This mini review follows the traditional narrative review study. According to these researches, essential oils are helpful in the treatment of malignancies, notably lung cancer. However, additional research, including clinical trials, is essential to enhance the treatment's efficacy.

1. Introduction

Cancer is a broad term that encompasses a range of illnesses that can attack anyone, whether by external factors or genetic inheritance. Cancer is a prominent cause of death globally. The most frequently reported new cases of cancer are breast cancer (2.26 million) and lung cancer (2.21 million), followed by colorectal cancer (1.93 million), prostate cancer (1.41 million), and skin cancer (1.2 million), and stomach cancer (1.09 million). When it comes to fatal cancer, lung cancer is extreme and away the most prevalent, with the World Health Organization (WHO) reporting 1.8 million cases in 2020 (Cancer, 2018; Cancer, 2021).

Lung cancer was classified into non-small cell lung cancer (NSCLC) and small cell lung cancer (SCLC), the more common type. NSCLC cases are more common than SCLC cases, accounting for approximately 80% to 85% of all lung cancer cases, whereas SCLC cases account for 15% to 20% of all cases. Despite its low prevalence, SCLC spreads more aggressively than non-small cell lung cancer (NSCLC) (What Is Lung Cancer? | Types of Lung Cancer, 2019). Lung cancer can be treated in many ways, such as immunotherapy, chemotherapy, targeted therapy, radiation therapy, surgery, and more. Cancer treatment options and suggestions depend on many factors, such as the type and stage of

cancer, potential side effects, the person's personal preferences, and overall health (What Is Lung Cancer? | Types of Lung Cancer, 2019). Each type of lung cancer treatment has risks and potential side effects, which should be considered. Adaptability to treatment depends on the individual's capacity to adapt to the prescribed regimen.

Food, clothing, and pharmaceuticals are all essential for human survival, as are other necessities such as water. Pharmaceutical products are the most critical because only certain prescription drugs can treat particular diseases or illnesses, making them the most critical. Islamic countries are expected to have approximately 1.9 billion people by the end of 2021, making Muslims the world's 2nd largest population group behind the Asian population (Muslim Population by Country 2021, 2021). The demand for *Halal* products is increasing worldwide, consequently with the expansion of the Muslim population. In terms of *Halal* food, which is the most fundamental necessity, there are several options available; *Halal* food is now freely available, and it was previously assumed that this would be adequate to meet demand from the community. In contrast, be it *Halal* or non-*Halal*, pharmaceutical products must be consumed depending on the patient's situation. Although Muslims believe that using any medicine is permissible, since treating the sickness is more important, due to religious beliefs, Muslims are more grateful for the effort put forth in seeking

Halal products.

What is a *Halal* therapeutic source, and how does it work? When using essential oils, is it permissible to use them in place of non-*Halal* therapeutic sources? Using essential oils as a *Halal* alternate treatment source for lung cancer can be beneficial, and this review aims to investigate that possibility. This mini review follows the traditional narrative review that provides an overview of the research findings on essential oils as an alternative *Halal* therapeutic source for lung cancer. This is the secondary study on reviewing the data from previous primary studies.

The following search terms were used with the AND Boolean search operator: "essential oil AND lung cancer," which yielded 266 results, and "*Halal* AND pharmaceutical," which yielded 85 results. The terms *Halal*, pharmaceuticals, anti-cancer, essential oils, and lung cancer were used as the article's keywords. The following search terms were used with the AND Boolean search operator: "essential oil AND lung cancer," which yielded 266 results, and "*Halal* AND pharmaceutical," which yielded 85 results.

2. Prohibited medicines in Islam

Haram (non-*Halal*) medicines were described as those containing substances prohibited from consumption or use under *Syari'ah* law (Islamic law). The most critical raw materials in the list of non-*Halal* for Muslims are any part from *Sus scrofa* spp. (boar/pig) and *Canis lupus* spp. (dog family), other than this, some materials and conditions cause the products as non-*Halal* products. Gelatine is one of the most debatable pharmaceutical chemicals on the market, and its use in *Halal* medicines should be considered. Gelatine is widely used in pharmaceuticals, both hard and soft capsules, and is made from collagen-derived animal protein. Apart from capsules, gelatine is also utilised to manufacture tablets and serums. Gelatine is frequently derived from porcine, as is bone and skin from cows (Halim *et al.*, 2015).

The utilisation of alcohol as a source of medication remains controversial for the production of *Halal* medicines. In Islam, alcohol is considered more harmful than beneficial. This prohibition applies to all illegal components used in the manufacture of the medicament. Other constituents, such as stearates (magnesium, calcium, and stearic acid), are often obtained from lard, or fatty acids obtained from pig stomachs and used as lubricants and binders, although they can also be obtained from plants. Ingredients such as glycerol, gelatine, heparin, ethanol, glycerine, and the enzyme trypsin are primarily produced from non-*Halal* sources (Annabi & Wada, 2016).

3. Alternative *Halal* therapeutic source

Halal medication was defined as containing only ingredients from sources permitted under Islamic law (*Syari'ah*). Rigorous adherence to the regulations specified above is required for all animals, plants, and organic or inorganic substances in all stages of their production and processing, including preparation, handling, packing, storage, and distribution (Khan & Shaharuddin, 2015). A pharmaceutical product is any chemical or preparation used to treat or prevent disease (O'Neil *et al.*, 2001). Pharmaceutical products are made up of a combination of active ingredients

and excipients, which combine to form the final product. This group of chemicals can be obtained from various sources, including animal, plant tissues, and synthetic sources (Maizirwan & MS, 2010).

Implants and medications produced from animals and humans are widely applied in medicine and surgery, yet health practitioners rarely have access to information about their constituents. At present, many pharmaceuticals on the market lack *Halal* logos. Additionally, sources regarding the *Halal* status of individual drugs are quite limited. As a result, it is difficult for health care professionals and patients to make pharmaceutical selection judgments. They have the right to know the *Halal* status of pharmaceutical products (Aziz *et al.*, 2014). This scenario, in some ways, heightens consumer awareness and concerns, particularly among those who adhere to strict eating practices, particularly Muslims, since everything is uncertain. To establish whether a drug has animal origins, it is possible to contact the manufacturer or a national medicine agency. However, the origin of the ingredients is not always obvious. Alternative medications, dressings, and implants are available that are not produced from humans or animals, such as those generated from plants or synthetics. This is not, however, available in all medicines (Eriksson *et al.*, 2013).

Fish skin gelatine from warm-water species may give a *Halal* alternative source of gelatine with nearly identical rheological qualities to mammalian gelatine and is a great way to recycle fish waste such as skin, bones, and fins (Akbar *et al.*, 2017). Nonetheless, vegetarians' demands have been met in recent years by introducing plant-based substitutions such as Hydroxypropyl Methylcellulose capsules (HPMC) and modified starch, the latter of which is *Halal* certified (Saha *et al.*, 2019; Zhang *et al.*, 2013). Aside from that, some of the additives may present a problem for Muslim consumers due to the absence of information about the constituents of their products. Excipients include dyes, fragrances, binders, emollients, fillers, lubricants, and preservatives (Regenstein *et al.*, 2003).

Plants are one of the few materials used to make 100% *Halal* ingredients; consequently, any products derived from plants are most advantageous. Natural chemicals from various plant species, including *Aquilaria malaccensis*, have been investigated as a potential alternative source of anti-inflammatory therapy (Eissa *et al.*, 2018). Years past, the consumption of chemical medicine and drug products shows some side effects to the patient, depending on the personal individual. Plants are one of the few raw materials guaranteed to be *Halal*. However, not all plants can be used the same way, as some plant species are hazardous and should not be consumed. For this reason, natural compounds, mainly from plant species, have been investigated as alternative pharmaceutical products for numerous diseases. According to researchers, researchers, various natural substances, particularly those derived from plant species, are currently being investigated as potential *Halal* medical treatments for various illnesses, including lung cancer.

4. Essential oils as *halal* therapeutic source

Essential oils (EOs) are plant-derived secondary metabolites that serve as natural protection opposing pathogens and other external conditions. They are also known as ethereal or volatile oils, and they contain a variety of distinct aromas

from which they can be extracted (Blowman *et al.*, 2018). EOs have a long history of being associated with various biological activities and being used in herbal medicine to treat various ailments. They seem to have a promising anti-cancer effect in long-term research (Gautam *et al.*, 2014). The study of EOs has generated considerable research interest due to their potential as anti-cancer agents, natural substances, and plant-based products that are considered *Halal*.

Plant-derived compounds are believed to be safer than synthetic compounds and provide a wide range of benefits in preventing chronic diseases and their symptoms. Due to the discovery that essential oils have chemopreventive potential, there has recently been considerable attention to exploiting EOs as pharmacological and therapeutic agents. The essential oil's ability to induce apoptosis in various tumor cell lines shows the indications for this. Some EOs showed remarkable anti-bacterial action against various facultative and obligate anaerobic bacteria. Moreover, these

constituents were discovered as the active chemicals responsible for the anti-oxidant capacity and anti-cancer activity of the EOs extracted from traditional medicinal plants (Cha *et al.*, 2010). According to multiple published publications, these EOs have been well-established for their naturally occurring qualities, which include anti-tumor, anti-biotic, anti-inflammatory, anti-oxidant, anti-viral, and anti-biotic capabilities, as well as their anti-bacterial and anti-viral properties (Ali *et al.*, 2015; Mitoshi *et al.*, 2012).

5. Application of essential oils as therapeutic agent for lung cancer

According to the World Health Organization, cancer is the leading cause of death worldwide, with lung cancer ranking among the top five cancers on the list. Some lung cancer cell lines were recorded among researchers, such as A549, NCI-H460, NCI-H1299, and NCI-H358 (Gautam *et al.*, 2014). The most popular cell line that was always mentioned is A549. Table 1 shows the list of plant species of essential oils with their main finding of mechanism.

Table 1: List of essential oils bearing plant species and the primary finding mechanism

No	Species	Cancer cell lines	Mechanism	Reference
1	<i>Cedrelopsis grevei</i>	A549	Cytotoxic	(Tardugno <i>et al.</i> , 2018)
2	<i>Artemisia dubia</i>	A549	Anti-oxidant, anti-cancer	(Shameem <i>et al.</i> , 2019)
3	<i>Pinus roxburghii</i>	A549	Cytotoxicity, anti-cancer, apoptosis, anti-inflammatory,	(Sajid <i>et al.</i> , 2018)
4	<i>Zingiber striolatum</i>	A549	Cytotoxic	(Tian <i>et al.</i> , 2019)
5	<i>Cirsium japonicum</i>	A549	Antitumor	(Ma <i>et al.</i> , 2019)
6	<i>Chrysanthemum boreale</i>	A549 and NCI-H358	Cytotoxic	(Chung <i>et al.</i> , 2019)
7	<i>Alpinia officinarum</i>	A549, NCI-H1975, NCI-H23, SPC-A1, NCI-H446,	Anti-cancer, apoptosis	(Li <i>et al.</i> , 2018)
8	<i>Perilla frutescens (L.) Britt.</i>	A549	Anti-oxidant, cytotoxic	(Chen <i>et al.</i> , 2020)
9	<i>Cymbopogon citratus</i>	LU134AM, LU135 and LU165	Apoptosis and cell proliferation	(Maruoka <i>et al.</i> , 2018)
10	<i>Lavandula dentata L.</i>	Calu-3 lung cancer cells	Cytotoxic, sedative, antidepressant, anti-bacterial, anti-oxidant, anti-fungal, carminative	(Justus <i>et al.</i> , 2019)
11	<i>Inula graveolens</i>	A549	Antiproliferative, cytotoxic	(Karan <i>et al.</i> , 2018)
12	<i>Cymbopogon citratus</i>	A549, NCI-H1975, NCI-H1650, NCI-H1299	Cytotoxic	(Trang <i>et al.</i> , 2020)
13	<i>Lippia alba</i>	A549	Cytotoxic	(Montero-Villegas <i>et al.</i> , 2018)
14	<i>Origanum minutiflorum</i>	A549	Anti-cancer, anti-oxidant, cytotoxic	(Sokmen <i>et al.</i> , 2020)
15	<i>Citrus reticulata</i>	A549	Apoptosis	(Castro <i>et al.</i> , 2018)
16	<i>Pelargonium capitatum</i>	NCI-H1299	Cytotoxicity, antitumor, necroptosis	(Yu <i>et al.</i> , 2019)
17	<i>Juniperus communis sp.</i>	A549	Cytotoxic	(Maurya <i>et al.</i> , 2018)
18	<i>Morinda citrifolia</i>	A549	Cytotoxic	(Rajivgandhi <i>et al.</i> , 2020)
19	<i>Arachis hypogaea</i>	A549	Anti-cancer, apoptosis	(Fazelifar <i>et al.</i> , 2021)

No	Species	Cancer cell lines	Mechanism	Reference
20	<i>Cedrelopsis grevei</i>	A549	Cytotoxic	(Tardugno <i>et al.</i> , 2018)
21	<i>Artemisia dubia</i>	A549	Anti-oxidant, anti-cancer	(Shameem <i>et al.</i> , 2019)
22	<i>Pinus roxburghii</i>	A549	Cytotoxicity, anti-cancer, apoptosis, anti-inflammatory,	(Sajid <i>et al.</i> , 2018)
23	<i>Zingiber striolatum</i>	A549	Cytotoxic	(Tian <i>et al.</i> , 2019)
24	<i>Cirsium japonicum</i>	A549	Antitumor	(Ma <i>et al.</i> , 2019)
25	<i>Chrysanthemum boreale</i>	A549 and NCI-H358	Cytotoxic	(Chung <i>et al.</i> , 2019)
26	<i>Alpinia officinarum</i>	A549, NCI-H1975, NCI-H23, SPC-A1, NCI-H446,	Anti-cancer, apoptosis	(Li <i>et al.</i> , 2018)
27	<i>Perilla frutescens (L.) Britt.</i>	A549	Anti-oxidant, cytotoxic	(Chen <i>et al.</i> , 2020)
28	<i>Cymbopogon citratus</i>	LU134AM, LU135 and LU165	Apoptosis and cell proliferation	(Maruoka <i>et al.</i> , 2018)
29	<i>Lavandula dentata L.</i>	Calu-3 lung cancer cells	Cytotoxic, sedative, antidepressant, anti-bacterial, anti-oxidant, anti-fungal, carminative	(Justus <i>et al.</i> , 2019)
30	<i>Inula graveolens</i>	A549	Antiproliferative, cytotoxic	(Karan <i>et al.</i> , 2018)

Reviewing some of the research papers on the anti-cancer properties of EOs concerning lung cancer cells reveals that there are different types of EOs, and that the mechanism of action is effective with different types of lung cancer cell lines, as revealed by the review. The cytotoxic effect of essential oils on cancer cell lines is the most frequently seen action method. In addition, essential oils have anti-oxidants, cancer prevention, anti-inflammatory, apoptosis, antitumor, sedative, anti-bacterial, anti-fungal, anti-depressant, anti-proliferative, necroptosis, and necrosis.

For some examples, the essential oil extracted from the flowers of *Artemisia dubia* was found to be highly concentrated in aroma chemicals such as terpene esters, sesquiterpenes, and oxygenated monoterpenes, with neryl-2-methylbutanoate (7.32%), 1,8-cineole (8.32%), and nerylisovalerate (9.79%) as their three primary chemical constituents. The oil had a substantial anti-proliferative effect against the human cancer cell lines HCT-116 and A549 (Shameem *et al.*, 2019). *Pinus roxburghii* essential oil (PREO) has been shown to reduce cell proliferation and cause apoptosis in cancer cells, an effect related to NF-B inhibition. At low concentrations, PREO induced cancer cell death and apoptosis. As a result, the use of PREO as an anti-cancer drug may be worth investigating *in vivo* (Sajid *et al.*, 2018).

The review study made multiple references to lemongrass essential oil (*Cymbopogon citratus*). Lemongrass, a member of the *Cymbopogon* genus, is a commonly used spice in tropical nations, particularly Southeast Asia. This species is a significant source of essential oils used in traditional medicine. Lemongrass has traditionally been used to treat gastrointestinal disorders. Lemongrass tea is an anti-inflammatory, analgesic, anti-fungal, and anti-bacterial agent. Several prior investigations have demonstrated that lemongrass essential oil possesses various pharmacological properties, including anti-bacterial, insecticidal, and cytotoxic properties. Citral was identified as the major constituent of lemongrass essential

oils. Additionally, the plant contains phenolics, flavonoids, ketones, terpenes, and alcohol (Maruoka *et al.*, 2018; Trang *et al.*, 2020).

The effects of lemongrass essential oil on various lung cancer cell lines have been investigated, including A549, LU134AM, LU135, LU165, NCI-H1650, NCI-H1299, and NCI-H1975. According to the review study, these EOs have apoptotic, anti-proliferative, and cytotoxic effects. (Trang *et al.*, 2020) researched the effects of various types of lemongrasses freshly picked from various regions throughout Vietnam on four types of lung cancer. They discovered that different types of lemongrass essential oil have different effects on the lung cancers studied (NCI-H1975, NCI-H1650, NCI-H1299, and A549) (Abdulhasan, 2021; Maruoka *et al.*, 2018; Trang *et al.*, 2020). Other essential oils have the same qualities as *Cymbopogon citratus*, *Artemisia dubia*, and *Pinus roxburghii* EOs.

6. Precaution using essential oils

Due to their low toxicity and use at the highest dose of 3% - 4% in a carrier oil, EOs were traditionally applied to the skin in conjunction with massage and were considered safe to use. In contrast, according to recent research, sensitization to EOs manifested as allergic contact dermatitis is increasingly becoming a significant source of concern among consumers. The latter is also airborne and can remain in the home long after all EOs have been removed due to their sequestering in furniture, walls, and other surfaces. On the other hand, consumers worry about sensitization to EOs in the form of skin irritation. The problem is that most unique and unusual phytols, plant extracts, and EOs have not been thoroughly studied for toxicity, mainly when applied to the skin or consumed. Additionally, exhaustive literature searches uncovered no scientific research examining their alleged therapeutic potential (Lis-Balchin, 1999).

With so much research on using EOs for self-care in various medical situations, the clinician must interpret such use so

that the patient understands the treatment goals. Whether conventional or alternative therapies are employed, healthcare providers must be prepared to support patients in all areas of health and well-being. Given that it is customary to ask patients about non-prescription drugs, herbal supplements, and prescription drug use during medication reconciliation, it may be prudent to extend consultation to include self-used essential oils. Self-guided aromatherapy requires a firm grasp on proper application (Which essential oils necessitate the use of a carrier oil? Which ones are OK for use undiluted? How may one obtain high-quality oils?) and guidance on how long it is safe to pursue self-care for minor ailments before consulting mainstream medicine. Clinicians can help ensure responsible use of essential oils by teaching patients about the limitations of Food and Drug Administration (FDA) essential oil regulation and the lack of valuable data and product safety (Manion & Widder, 2017).

7. Conclusion

The rapid growth of the *Halal* pharmaceutical sector demonstrates how religion can be a motivating element that, when properly utilized, may create significant economic benefits. Plant-based products are a desirable alternative to *Halal* items. Given the extent and importance of the *Halal* pharmaceutical sector, there will be a need to establish further *Halal* therapeutic alternatives in the future, particularly for cancer. Many researchers have been intrigued by the EOs derived from plants; they have been used to cure various ailments since antiquity. According to these researches, EOs help treat malignancies, notably lung cancer. Apart from serving as a *Halal* substitute for pharmaceutical products, EOs can also serve as a supplement to chemical products that may produce adverse customer reactions. Additional research, including clinical trials, is essential to enhance the treatment's efficacy. Future investigations, both qualitative and quantitative, are advised to supplement this conceptual inquiry. This is critical, especially when it comes to ensuring the safety of EOs and avoiding any other health concerns associated with their use.

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