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Exploring the pharmacological role of cuminaldehyde: A review

Duraisamy Kannan, *Leelavinothan Pari
Department of Biochemistry & Biotechnology, Faculty of Science, Annamalai University, Annamalainagar, Tamil Nadu, India

Abstract
Medicinal plants and their phytochemicals are used traditionally to cure diseases. Cuminaldehyde is an essential oil of a natural organic compound mostly found in plants like *Cuminum cyminum, Cinnamomum verum, Carum carvi, Cinnamomum cassia and Bunium persicum,* and has shown anticancer, antiplatelet, antibacterial, antifungal, antidiabetic, antimalarial and ameliorating symptoms of Parkinson's disease. Essential oils are less dangerous than chemical medicines. Cumin (*Cuminum cyminum*) commonly known as Jeera is used in the household flavoring agents, native from East Mediterranean to the Indians. The most important chemical composition of the cumin essential oil was cuminaldehyde. *Cinnamomum verum, Cuminum cyminum* both plant seed used as a conventional Chinese herbal medicine, particularly a cuminaldehyde, an important herbal medicine found in true cinnamon tree's bark shows anticancer effect.

Keywords: cuminaldehyde, antimicrobial, anti-inflammatory, antioxidant, antidiabetic

Introduction

Cuminaldehyde (4-isopropylbenzaldehyde) a natural monoterpenoid. It is a benzaldehyde with an isopropyl group substituted in the 4th-position. Cuminaldehyde commonly found in commelinid plants such as *Cuminum cyminum, Cinnamomum verum, Carum carvi, Cinnamomum cassia and Bunium persicum. Carum carvi and Cuminum cyminum,* it's used as folk medicine in Asia, Europe, and Africa.

Cuminum cyminum plant seed is used as the flavoring agent. They are also used as a hunger stimulant and to ease numerous stomach disorders [1]. *Cuminum cyminum* plant seed has micro nutrients include about, high amount of potassium and magnesium, low amount of iron. Magnesium serves a crowd of functions, like promoting heart health, promotes the absorption of calcium, and controlling blood pressure. Cumin seeds have been found to have essential oils such as cuminaldehyde (4-isopropyl benzaldehyde), plant pyrazines, 2 ethoxy-3-isopropyl pyrazine, and 2-methoxy-3-Sec-butyl pyrazine [1].

Cuminaldehyde has also been found in high amount in other frequently used spices such as true and Black Zaire [2], Cinnamon tree [3] Cumin is traditionally used to relieve abdominal colic [4], treat heartburn [5, 6], diarrhea and jaundice [7]. It also has antibacterial [8], antioxidant [9, 10], and antifungal effects [11]. Anticonvulsant activity of cumin oil was also [12].

Moreover, *Cuminum cyminum* plant seeds have numerous photochemical that are known to have antioxidant, and anti-flatulent properties. The active probity in the cumin may increase the motility of the gastrointestinal (GI) tract, as well as the increase the digestion power by increase GI enzyme secretions. Cumin seeds contain an excellent source of minerals and also has rich amounts of vitamins like B-complex vitamins such as thiamin, riboflavin, vitamin B-6, niacin, and other antioxidant vitamins like vitamin E, vitamin C, and vitamin A [1].

The aim of this review is to provide the structured outline about natural sources, Biochemical metabolism, and different applications of cuminaldehyde in the pharmaceutical, biomedical, food, and other industries, which will provide enormous information to a wide range of researchers, working on the different applications of natural products.

Biological and Pharmacological Activity

Antimicrobial activity

Cuminaldehyde is one among the major flavor components of cumin essential oil that can stimulate different biological activities [13]. Cuminaldehyde has good antimicrobial activities against multidrug resistant strains of *Salmonella spp, S. typhi Vi-positive, S. typhi Vi-negative, and S. paratyphi* followed by moderate activities against *E. coli, S. aureus,* and *B. licheniformis* strains. It was also reported to have strong growth inhibitory effect particularly with MDR E. coli SS1 strain as observed on TLC plates with big inhibition zone in case of *E. coli, S.typhi, S.paratyphi, S.aureus, B.licheni formis* [14, 15].

Table 1 shows the MIC of cuminaldehyde against different Bacteria such as *Staphylococcus aureus, Bacillus subtilis, Bacillus cereus, Bacillus coagulans, Escherichia coli, Enterobacter aerogenes, Pseudomonas aeruginosa* [16].

Table 1. MIC (mg/ml) of cuminaldehyde towards Bacteria

Organism	Cuminaldehyde
Bacteria	2.0
Staphylococcus aureus	
Bacillus subtilis	0.75
Bacillus cereus	0.75
Bacillus coagulans	1.0
Escherichia coli	0.75
Enterobacter aerogenes	1.5
Pseudomonas aeruginosa	3.25

Antifungal activity

Head space sampling and gas chromatography-mass spectrometry analysis of black cumin identified seven volatile compounds, γ-terpinene, limonene, p-cymene, β-pinene, α-pinene, cuminaldehyde, and myrcene. Among these, cuminaldehyde and p-cymene showed the strongest antifungal activities against *F. oxysporum.*

The same compounds also showed the antifungal activities against soil-borne phytopathogenic fungus *Verticillium dahlia*, and foliar phytopathogenic fungi such as *Botrytis cinerea*, *Alternaria Mali* [17], *Aspergillus nige, A. flavus, A. parasiticus, Penicillium chrysogenum.*and

Yeasts, such as *Saccharomyces cerevisiae and Candida ufilis*. Table 2 shows the cuminaldehyde have most potent antifungal activity. In general, fungal and yeast cultures were more sensitive to cuminaldehyde than the bacteria [16].

Table 2: MIC (mg/ml) of cuminaldehyde towards Fungi and Yeasts

Fungi	0.05
Aspergillus niger	
A. flavus	0.05
A. parasiticus	0.10
Penicillium chrysogenum	0.025
Yeasts	0.025
Saccharomyces cerevisiae	
Candida ufilis	0.025

Anti-inflammatory activity

Inflammation is a normal defensive response to tissue injury or infection induced through an invasive struggle of microorganisms and non-self-cells in the body (host) and eliminates dead or injured host cells. However, chronic and extreme inflammations could cause many inflammatory diseases, such as cancers, rheumatoid arthritis, atherosclerosis, periodontitis, and chronic hepatitis [18, 19]. Cuminaldehyde has been generally accepted that the excessive production of pro-inflammatory cytokines and mediators, such as interleukin-1 (IL-1), IL-6, tumor necrosis factor-α (TNF-α), nitric oxide (NO), and prostaglandin E2 (PGE2), playing effective roles in the development of these inflammatory diseases.

Cumin essential oil (CuEO) extracted from the seeds was employed to investigate the anti-inflammatory effects of lipopolysaccharide- (LPS-) stimulated RAW cells and the potential therapeutic approaches could help to regulate the expression of these proinflammatory genes and it would be useful for the treatment of many chronic diseases with an underlying inflammatory origin [20]. The cumin essential oil (CuEO) containing cuminaldehyde has attracted great attention during the last few years due to its robust bio-active properties, including anti-inflammatory role [21].

Antimalarial Activity

The potent antimalarial activity of cuminaldehyde was evaluated [22, 23] and there is no strong structural resemblance between cuminaldehyde and monoterpenoids with proven antiplasmodial activity. In comparison to other monoterpenoids, cuminaldehyde is special because of its aromatic ring and makes it be similar to phenyl propanoids. The phenyl propanoids posses antimalarial activity [24], so there may be more chances to produce antimalarial effects of cuminaldehyde due to structural resembles.

Antioxidant Activity

Cuminum cyminum plant flowers had phenolic compounds and important fats, which scavenge the free radicals and prevent the lipid per oxidation. The collective activities of Cuminaldehyde (4-isopropylbenzaldehyde) and para-cymene on DPPH radical effects (1, 1 - diphenyl 2-picryl hydroxyl) were studied in the liver tissue. The results showed that cumin aldehyde and para-cymene enhancing the DPPH radical scavenging activity [25]. Cuminaldehyde had a significant enhancer effect of SOD, catalase, and glutathione peroxidase activity and the net results showed that cuminaldehyde have to enhance free radical scavenging activity. The cuminaldehyde, para cumin, and para-cymene increased antioxidant enzyme such as superoxide dismutase, catalyses and glutathione peroxides [26].

Since high cumin phenolic content and essential fats derived from *Cuminum cyminum* plant seed could maintain the redox balance by its antioxidant (native free radical scavenging) and antioxidant enzyme regulating activities, this plant can be used as a good source of nutrition to protect the body from redox stress. Therefore, certain concentration ranges of cumin aldehyde and para-cymene can be used in order to protect a liver against ROS driven diseases.

Antifibrillation Activity

Fibrillation of alpha-syncline (α-SN) is a critical process in the pathophysiology of several neurodegenerative diseases, especially in Parkinson's disease. Application of bioactive inhibitory compounds from herbal extracts is a potential therapeutic approach to this cytotoxic process. In evaluation with baicalein, have well-known inhibitor of α-SN fibrillation, The presence of spermidine, an α-SN fibrillation inducer, dominantly enforced the inhibitory effects of cuminaldehyde even more intensively than baicalein. Cuminaldehyde prevents α-SN fibrillation even in the presence of cumin seeds [27, 28].

The cuminaldehyde show the no toxic effect on PC12 cells. Cuminaldehyde is a harmless compound, treated with α-SN fibrillation showed no toxic effects on the cells showed that cuminaldehyde, can modulate α-SN fibrillation. Hence, suggesting that such natural active aldehyde could have potential therapeutic applications [29]. Regarding the inhibitory activity of cuminaldehyde was also compared with 2 chemically virtually similar compounds, p-cymene and limonene, and a well-known inhibitor of amyloid fibrillation, baicalein. The net result showed cuminaldehyde was the most abundant compound on α-SN fibrillation directly [30].

Anticarcinogenic / antimutagenic activity

The cuminaldehyde activate the both caspase-3 and -9, and morphological features of apoptosis. cuminaldehyde also led to lysosomal vacuolation with an up regulated volume of acidic compartment and cytotoxicity, together with inhibitions of both topoisomerases I and II activities. The additional study shows that the anticancer activity of cuminaldehyde was experiential in the model of nude mice. Cuminaldehyde involved the suppression of cell proliferative markers, topoisomerase I as well as II, together with the increase of pro-apoptotic molecules, associated with up regulated

lysosomal vacuolation [31].

Cuminaldehyde (CuA) from *Cinnamomum verum* and *Cuminum cyminum*, suppressed explosion and induced apoptosis as indicate by an up-regulation of pro-apoptotic bax and bak genes and a down-regulation of anti-apoptotic bcl-2 and bcl-XL genes, mitochondrial membrane potential loss, cytochrome c release, activation of caspase 3 and 9, and morphological characteristics of apoptosis, including blebbing of the plasma membrane, nuclear condensation, fragmentation, apoptotic body formation. The growth-inhibitory effect of cuminaldehyde was also evident in a nude mice model, NCI-H520 cells, human lung adenocarcinoma A549 cells and colorectal adenocarcinoma COLO 205 suggest that cuminaldehyde could be a prospective agent for anticancer therapy [32].

Antidiabetic activity

Diabetes mellitus (DM) affects 300 million people worldwide and is the leading cause of blindness, kidney malfunction, heart attack, and amputation among adults [33]. Achieving blood-glucose levels as close to normal as possible has been measured as one of the major goals of therapy for those suffering from diabetes mellitus, as a high blood-glucose level is implicated in the development of macro- and micro vascular complication associated with diabetes [34]. However, in clinical practice, normalizing blood-glucose levels are a formidable challenge. Even more difficult is the control of postprandial hyperglycemia [35]. Fortunately, both dietary and pharmacological tools are now available for its management. DM is a multi-factorial disease, the available pharmaceuticals, despite their sensible treatment, target mostly one pathway to control hyperglycemia and encounter several side effects. Therefore, new therapeutic paradigms aim to hit several pathways using only one agent such as ant diabetic plants and their phytochemicals may fulfill this need.

One active principle was isolated from the cumin oil as cuminaldehyde demonstrated significant but relatively lower inhibitory effects on aldose reductase and alpha glucosidase than an orally approved antidiabetic drug Acarbose [36]. Cumin controlling the free radical production of diabetic rats with cumin leads to decreasing the blood glucose, glycosylated hemoglobin, creatinine and blood urea levels within 28 days, cumin significantly decrease the oxidative stress on the liver and kidney tissues. In other words, cumin improved the liver and kidney antioxidant status of diabetic's mic [37, 38].

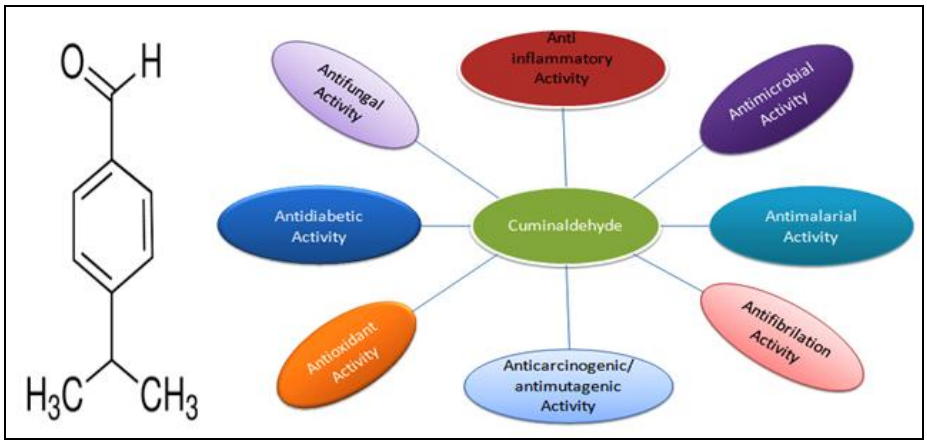

Fig 1: (a) Structure of Cuminaldehyde, (b) Pharmacological Activity of Cuminaldehyde.

Conclusion

Cuminaldehyde (4-isopropylbenzaldehyde), is a natural, biologically active constituent of *Cuminum cyminum.* Its work against various diseases and there needs to do proper work for the drug preparation which is easily available in the market with low cost.

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