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Original Article

Selected essential oils inhibit key physiological enzymes and possess intracellular and extracellular antimelanogenic properties *in vitro*

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ABSTRACT

Essential oils (EOs) extracted from six medicinal herbs and food plants [*Cinnamomum zeylanicum*, *Psiadia arguta*, *Psiadia terebinthina* (PT), *Citrus grandis* (CGp), *Citrus hystrix* (CH), and *Citrus reticulata* (CR)] were studied for any inhibitory potential against key physiological enzymes involved in diabetes (α-glucosidase), skin aging (collagenase and elastase), and neurodegenerative disorders (acetylcholinesterase). Kinetic studies of the active EOs on the aforementioned enzymes were determined using Lineweaver–Burk plots. The intracellular and extracellular antimelanogenic potential of the EOs were evaluated on B16F10 mouse melanocytes. CH and CR were found to significantly inhibit (2.476 ± 0.13 μg/mL and 3.636 ± 0.10 μg/mL, respectively) acetylcholinesterase, compared with galantamine (3.989 ± 0.16 μg/mL). CH inhibited collagenase (50% inhibitory concentration 28.71 ± 0.16 μg/mL) compared with the control (24.45 ± 0.19 μg/mL). The percentage inhibition in the elastase assay of CH was 63.21% compared to the positive control (75.09%). In addition, CH, CR, CGp, *Cinnamomum zeylanicum*, and PT were found to significantly inhibit α-glucosidase (276.70 ± 0.73 μg/mL, 169.90 ± 0.58 μg/mL, 240.60 ± 6.50 μg/mL, 64.52 ± 0.69 μg/mL, and 313.0 ± 5.0 μg/mL, respectively), compared to acarbose (448.80 ± 0.81 μg/mL). Active EOs showed both uncompetitive and competitive type of inhibition. The EOs also inhibited intracellular (50% inhibitory concentration 15.92 ± 1.06 μg/mL, 23.75 ± 4.47 μg/mL, and 28.99 ± 5.70 μg/mL for CH, CR, and CGp, respectively) and extracellular (< 15.625 μg/mL for CH, CR, CGp, and PT) melanin production when tested against B16F10 mouse melanocytes. Results from the present study tend to show that EOs extracted from these medicinal

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plants can inhibit key enzymes and may be potential candidates for the cosmetic and pharmaceutical industries.

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1. Introduction

Essential oils (EOs), also known as ethereal oils [1,2], are obtained mostly from vegetable organs (flowers, leaves, barks, woods, roots, rhizomes, fruits, and seeds) through different processes such as expression, fermentation, enfleurage, or extraction [3,4]. Although their composition consist mainly of terpenes, terpenoids, and phenylpropanoids, they represent a great diversity of chemical structures, chemical compositions, and for that matter, an assortment of properties.

EOs available on the market are mostly known for their odoriferous potential, while they can also be used in the management of many diseases [5–7]. EOs being rich in polyphenolic and terpenes components can be exploited for their potential antimicrobial, antioxidant, and anti-inflammatory properties. For instance, lavender oils, which are rich in linalool and linalyl acetate, can be found in approved drugs, for the treatment of anxiety disorder. Also, it has been purported that the use of EOs extracted from citrus fruits, rosemary, lavender, and others can be valued as effective antimicrobials, which has confirmed their use as natural preservatives in cosmetic products as well as food additives in food [8–10]. However, some components of EOs such as safrole and estragole, can also be deleterious for humans. The use of EOs thus needs to be documented and tested accordingly prior to use.

Noncommunicable diseases (NCDs) such as diabetes, cardiovascular diseases, neurodegenerative diseases, and other metabolic disorders have been reported by the World Health Organization [11] to be responsible for the death of > 38 million people every year, and 28 million of these fatalities occur in middle-income countries. Recent studies have been dedicated to the inhibition of key enzymes involved in pathologies as an effective strategy for the treatment and management of NCDs [12–15]. For instance, acetylcholinesterase (AChE) inhibition has been investigated in the management of neurodegenerative disorders such as Alzheimer's disease (AD), due to its potential to impede the cholinergic deficit that is associated with the cognitive dysfunction occurring in AD [14]. AD is a disease that concerns ~5% of the population in developed countries. Research into its symptoms, causes, risk factors, and treatment has gained an impact in recent decades. The progression of AD has also been linked to oxidative stress. Studies have showed a relationship of free radicals with the pathology of neuronal death similar to that in AD [16]. It has also been purported by Madeo and Elsayed [14] that there is a relationship between oxidative stress and AD, as the level of peripheral markers of oxidative stress is reported to increase with the severity of the cognitive disorder.

The management of type 2 diabetes has also been documented in the literature through the actions of natural plant products, involving two major techniques. First, the scavenging of free radicals, since diabetes have been correlated to a defective antioxidant defense system and an increase in level of free radicals [17]. Second, the inhibition of key enzymes involved in the breakdown of starch, such as α-amylase and α-glucosidase, which help reduce glucose level in the blood. These two key enzymes are therapeutic targets in the management of diabetes. Their involvement in the breakdown of starch to glucose leads to an increase in blood glucose level. In contrast, inhibition of these enzymes leads to a delay in glucose absorption and thus regulating postprandial glucose level in the bloodstream.

Oxidative stress has been purported as one of the mechanism associated with oxidative damage triggered by free radicals and leading to chronic pathology like neurodegenerative diseases, diabetes, loss of skin elasticity, cancer, and coronary heart diseases. Aging as a skin degradation process has been categorized as the intrinsic and extrinsic aging process. Intrinsic aging refers to the changes in elasticity of the skin, which is a natural process occurring with time, while extrinsic aging is a result of overexposure of the skin to harmful UV radiation, leading to alteration of the connective tissue due to the formation of peroxides, reactive oxygen species, and other components [18].

Tropical islands like Mauritius are endowed with rich floral biodiversity having an interesting microcosm with diverse species including aromatic medicinal plants, offering interesting biological activities. Aromatic and medicinal plants have been scrutinized in the quest for alternative natural bioactive products and drugs. Drugs used for the management of diseases have shown positive results, especially for patients with AD, for which no cure exists to date. However, these drugs are also associated with several major adverse effects. Compounds such as galantamine and tacrine for AD, along with acarbose and voglibose used against diabetes mellitus have shown adverse effects leading to gastrointestinal disease and hepatotoxicity. Thus, the search for new phytomedicines that can inhibit key physiological enzymes is warranted. The present study was designed to evaluate the efficacy and the potential of EOs extracted from medicinal plants used in traditional medicine to inhibit key enzymes involved in several NCDs.

2. Methods

2.1. Collection of plant materials

Exotic and endemic plants included in the present study are those used traditionally by the local people as medicinal herbs

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