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Pharmacotherapeutic potential of ginger and its compounds in age-related neurological disorders

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Abstract

Age-related neurological disorders (ANDs), including neurodegenerative diseases, are multifactorial disorders with a risk that increases with aging. ANDs are generally characterized by common neuropathological conditions of the central nervous system, such as oxidative stress, neuroinflammation, and protein misfolding. Recently, efforts have been made to overcome ANDs because of the increase in age-dependent prevalence. Ginger, the rhizome of *Zingiber officinale* Roscoe, is a popular food spice and has a long history of use in traditional medicine for treating various disease symptoms. The structure-activity relationships of ginger phytochemicals show that ginger can be used to treat ANDs by targeting different ligand sites. This review shows that ginger and its constituents, such as 6-gingerol, 6-shogaol, 6-paradol, zingerone, and dehydrozingerone, are effective for ameliorating the neurological symptoms and pathological conditions of ANDs through by modulating cell death or cell survival signaling molecules. From this review, we conclude that the active ingredients in ginger have therapeutic potential in ANDs.

Introduction

Aging is a primary risk factor for many neurological disorders because brain tissue is more vulnerable to aging insults than other organs (Wyss-Coray, 2016). Age-related neurological disorders (ANDs) include neurodegenerative diseases (NDDs), such as Alzheimer's disease (AD) and Parkinson's disease (PD), as well as other ANDs such as migraine and epilepsy (Jove et al., 2014, Mattson and Magnus, 2006). ANDs are characterized as multifactorial disorders that have common pathological features including neuronal loss, neuroinflammation, oxidative stress, and abnormal protein aggregation in the central nervous system (CNS) (Buendia et al., 2016, Jove et

al., 2014, Mattson and Magnus, 2006). These disorders have been a large burden on public health due to an increase in the aging population, which is at high risk for onset of several diseases according to the Global Burden of Disease Study (Silberberg et al., 2015, Thakur et al., 2016).

With no established cure, only a few drugs have been approved for the treatment but not prevention of ANDs (Bhullar & Rupasinghe, 2013). The existing AND drugs exert only symptomatic effects primarily by modulating neurotransmission (Berg, Belnoue, Song, & Simon, 2013). For example, three out of the five AD drugs are acetylcholinesterase (AChE) inhibitors, and the majority of PD drugs are levodopa or dopamine (DA) agonists (Anand et al., 2014, Samudra et al., 2016). Despite enormous efforts and cost to identify a candidate drug that interacts with a single target with high specificity, or simultaneously regulates multiple targets via chimeric moieties for decades, there is still an unmet need for pharmacotherapeutic agents for ANDs (Bottegoni et al., 2012, Dias and Viegas, 2014, Zheng et al., 2014).

Natural products (NPs) include a variety of chemical compounds that have been evolutionarily selected for their ability to enhance the survival of an organism (Brahmachari, 2013). Due to diverse biological activities, they have widely been applied for human healthcare as a dietary supplement or traditional medicine for thousands of years (Ekor, 2014). Promising approaches for AND drugs may include identifying NPs that possess multiple pharmacological activities on different targets and validate them. Given that they contain a diversity of compounds in terms of structure and biological activity, NPs are likely to have a broader range of targets than synthetic compounds (Harvey et al., 2015, Koehn and Carter, 2005). In a systems-based approach, it was revealed that compounds derived from NPs are structurally more similar to human metabolites than conventional small-molecule drugs (Kim, Ryu, Lee, & Lee, 2015). This systematic approach may provide clues to the potentials of NPs for multi-target activities. Thus, NPs may be one of promising strategies for protecting and treating multifactorial diseases, such as ANDs, due to their multi-targeting actions with multiple components (Harvey et al., 2015, Koehn and Carter, 2005). Actually, the remarkable synergistic actions of ginger have been demonstrated. Orally fed ginger extract exhibited 2.4-fold higher anti-proliferative effects than an artificial mixture of ginger-derived compounds in human prostate tumor xenografts (Gundala et al., 2014). This result may be explained by the synergistic actions among active ginger compounds compared to the actions of each compound alone (Brahmbhatt, Gundala, Asif, Shamsi, & Aneja, 2013).

Recently, the evidence about the neuropharmacological effects of ginger has been accumulated. Here, after a brief overview of ginger, we reviewed the pharmacotherapeutic actions and the underlying mechanisms of ginger and its active compounds in ANDs and ANDs pathological conditions.

Section snippets

Ginger and its compounds

Ginger, the rhizome of *Zingiber officinale* Roscoe (Zingiberaceae family), is a widely used food ingredient and has been frequently prescribed for curing various symptoms, such as the common cold, nausea, asthma, cough, bleeding, and muscle pain in traditional medicine (Mascolo et al., 1989, Wang and Wang, 2005). Ginger has been also combined with other

prescription drugs for brain diseases, such as paralysis by ischemic stroke and a nerve sedative (Xutian, Tai, & Yuan, 2014). Moreover, it has…

Neuropharmacological actions of ginger in ANDs

Accumulated evidence shows that ginger and its compounds have neuropharmacological actions in ANDs, such as AD and dementia, PD, stroke, multiple sclerosis (MS), migraine, and epilepsy as well as ANDs pathological conditions (Table 1, Table 2)….

Summary and perspectives

In this review, we discussed the current evidence for the pharmacological potential of ginger and its compounds in the treatment of ANDs (Fig. 3). Ginger has been validated for its therapeutic efficacy not only in AND models but also in ANDs-related pathological conditions. It ameliorates disease-specific symptoms and pathological changes by controlling the pathogenesis of ANDs. Furthermore, ginger-derived active compounds, including 6-gingerol, 6-shogaol, zingerone, dehydrozingerone, and…

Conflict of interest statement

The authors declare that there are no conflicts of interest….

Acknowledgments

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Dextran-coated iron oxide nanoparticles in combination with ginger extract without NGF promote neurite outgrowth and PC12 cell branching
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Enhancement of 6-gingerol extraction from Bentong ginger using supercritical carbon dioxide
2023, Journal of CO2 Utilization

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Metabonomics and the gut microbiome analysis of the effect of 6-shogaol on improving obesity
2023, Food Chemistry

Citation Excerpt :

...As 6-gingerol is easily dehydrated to form 6-shogaol under high temperature and low pH, 6-shogaol is the highest gingerols component in dried ginger (Ko et al., 2019). Studies have shown that shogaols have higher biological activity than their precursor gingerols (Choi et al., 2018). Several animal studies and clinical trials have demonstrated in recent years that the potential anti-obesity effect of ginger (Vahideh et al., 2018; Seo et al. 2021; Park and Jung, 2020)....

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Ginger essential oil: Chemical composition, extraction, characterization, pharmacological activities, and applications

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Phytomedicine, Volume 43, 2018, pp. 28-36

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6-Shogaol has anti-amyloidogenic activity and ameliorates Alzheimer's disease via CysLT1R-mediated inhibition of cathepsin B

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