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Review

Literature review of 10 plants products for their anti-inflammatory, antioxidant, immunomodulatory, and antiviral properties

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ABSTRACT

The global health pandemic of coronavirus disease (Covid-19) did not have specifically approved medication for the treatment. To maintain the human immunity power by natural remedies is the only way to prevent coronavirus infection. We designed a study protocol by selecting 10 natural plant active constituents that were claimed by traditional and investigational ways to have anti-inflammatory, antioxidant, immunomodulatory, and antiviral properties. We will analyze these selected 10 plants' active constituents by molecular docking analysis. This article is a literature review of selected 10 plants products including *Coffea Arabica, Curcuma longa, Glycyrrhiza glabra, Zizyphus vulgaris, Sisymbrium irio, Borago officinalis, Althaea officinalis, Malva sylvestris, Cordia Latifolia,* and *Adhatoda vasica* for their anti-inflammatory, antioxidant, immunomodulatory, and antiviral properties.

Introduction

An extensive literature review was made by using PubMed and PubChem database on selected 10 plants products including *Coffea Arabica, Curcuma longa, Glycyrrhiza glabra, Zizyphus vulgaris, Sisymbrium irio, Borago officinalis, Althaea officinalis, Malva sylvestris, Cordia Latifolia,* and *Adhatoda vasica* for their anti-inflammatory, antioxidant, immunomodulatory and antiviral properties.

Coffea Arabica

Coffee has been studied for its health benefits, including the prevention of several chronic diseases, such as type 2 diabetes mellitus, cancer, Parkinson's, and liver diseases. Chlorogenic acid (CGA), an important component in coffee beans, was shown to possess antiviral activity against viruses.[1] *Coffea arabica* extract (CAE) containing 48.3 ± 0.4 mg/g of chlorogenic acid and a trace amount of caffeic acid was found to alleviate photoaging activity in human skin fibroblasts. In this study, polyphenol-rich CAE was investigated for its antioxidant and anti-inflammatory properties.[2] Many pharmacological activities are attributed to these components that include anti-oxidant, anti-inflammatory, immunomodulatory, anti-microbial, anti-cancer, cardioprotective, and neuroprotective effects.[3] In one study, the antioxidant performance, nutritional composition, long-distance transport of Se, photosynthetic

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pigments, and growth of *Coffea arabica* genotypes in response to Se concentration in solution were evaluated. These results suggest that antioxidant metabolism was effective in regulating oxidative stress in plants treated with Se. The increase in sucrose, and decrease in SOD, CAT, and ascorbate peroxidase (APX) activities, as well as Se compartmentalization in the roots, were the main biochemical and physiological modulatory effects of coffee seedlings under stress conditions due to excess of Se.[4] The expression of mRNA for tumor necrosis factor-alpha and interleukin-6 was decreased in cells treated with the coffee extracts and the expression decreased with increasing roasting levels. These data suggest that coffee has physiological antioxidant and anti-inflammatory activities and these effects are negatively correlated with roasting levels in the cell models.[5]

Curcuma longa

One study revealed the potential antiviral activity of *Curcuma longa* against H9N2 influenza viruses and can be opted as an alternative to antibiotics and antiviral drugs to minimize the antimicrobial resistance in the human and animal population.[6] Human studies have found some evidence of the anti-inflammatory activity of curcumin. The laboratory studies have identified many different molecules involved in inflammation that are inhibited by curcumin including phospholipase, lipooxygenase, cyclooxygenase 2, leukotrienes, thromboxane, prostaglandins, nitric oxide, collagenase, elastase, hyaluronidase, monocyte chemoattractant protein-1, interferon-inducible protein, tumor necrosis factor (TNF), and interleukin-12 (IL-12). Curcumin has been demonstrated to be safe in six human trials and has demonstrated anti-inflammatory activity. It may exert its anti-inflammatory activity by inhibiting many different molecules that play a role in inflammation.[7] Curcumin (diferuloylmethane) is an active ingredient in turmeric (*Curcuma longa*) with anti-inflammatory, antioxidant, chemopreventive, chemosensitization, and radiosensitization properties. Conjugation of curcumin (Curc) to albumin (Alb) has been found to increase the aqueous solubility of the drug. Results of the present study suggest that curcumin albumin conjugate has immunomodulatory and tumor growth inhibition properties.[8]

Glycyrrhiza glabra

In one study the effect of extracts from *Glycyrrhiza glabra* leaves was investigated against Newcastle disease virus (NDV) by an in-vivo assay. Seven groups of nine-day-old embryonated chicken eggs were inoculated with various treatments of different plant extracts. Results have verified that all the extracts especially that of methanol 300µg/mL from leaves of *Glycyrrhiza glabra* have strong antiviral activity against NDV in vivo.[9] Pharmacological experiments have demonstrated that different extracts and pure compounds from this species exhibit a broad range of biological properties, including antibacterial, anti-inflammatory, antiviral, antioxidant, and antidiabetic activities.[10] One study analyzed the molecular interactions of protein-phytocompounds, by AutoDock Vina 4.2 tools. The best interactions of each algorithm were subjected to molecular dynamic (MD) simulations to have an insight into the molecular dynamic mechanisms involved. Selected phytoconstituents gave a good score for binding affinity with the main protease 6LU7 of SARS CoV-2 as compared to the antiviral drugs already being used in the disease therapy.[11]

Zizyphus vulgaris

In recent years, jujube fruit (*Zizyphus vulgaris* L.) has been reported to have anti-inflammatory effects as a traditional therapeutic agent. Therefore, the study was conducted to investigate the effects of jujube fruit extract on second-degree burn wounds among Balb/c mice. The results of the study indicated that the jujube fruit extract could accelerate burn wound healing among Balb/c mice.[12]

A pilot study revealed that a 40 µl dose of 10^7 CFU/ml could induce infection which persists up to 08 days post-infection. Mice treated with T. vulgaris and Z. jujuba showed a reduction in gross lesion score of both heart and lungs. Treatment with only some plants could significantly decrease the bacterial load of the throat (T. vulgaris) heart, blood, and joint (C. latifolia, and T. vulagris). This was the first report confirming in vivo anti-MRSA potential of C. latifolia and T. vulgaris and highlight the need to explore bioactive constituents of these plants.[13]

Sisymbrium irio

Crude extracts of the seeds of *Sisymbrium irio* L. were tested for antipyretic, analgesic, and antimicrobial effects. The ethanolic extract exhibited significant antipyretic (Onset: < 1 hour, peak: 3 hours, duration: > 5 hours; $p < 0.05$) and analgesic ($p < 0.001$) effects. It also exhibited marked antibacterial action against both gram-positive and gram-negative organisms and was found to be nontoxic in acute studies.[14] To combat the multidrug-resistant (MDR) superbugs, silver nanoparticles (Ag NPs) were synthesized using an aqueous leaf extract of seasonal desert plant *Sisymbrium irio* obtained from the central region of Saudi Arabia by a simple one-step procedure. The physical and chemical properties of the Ag NPs were investigated through ultraviolet-visible analysis (UV-vis), Fourier-transform infrared (FTIR) spectroscopy, X-ray diffraction (XRD), scanning electron microscope (SEM), and transmission electron microscope (TEM) analysis. In conclusion, the newly synthesized Ag NPs could be a potential alternative candidate in biomedical applications in controlling the spread of MDR pathogens.[15]

Borago officinalis

Antioxidant activity of *Borago officinalis* was evaluated by using a 2, 2-diphenyl-1-picryl-hydrazyl-hydrate assay. The data of the study showed that the extracts of *Borago officinalis* possess antioxidant and free radical scavenging activities.[16] Borage (*Borago officinalis*) is a plant with nutritional value that is also used in traditional medicine to treat gastrointestinal diseases. The study investigated the amoebicidal activity of a methanol extract of borage. The 50% inhibitory concentration (IC_{50}) of the extract for Entamoeba histolytica was 33 µg/mL. The 50% lethal dose of the extract for brine shrimp was greater than 1,000 µg/mL. The IC_{50} of the extract for Vero cells was 203.9 µg/mL. These results support the use of borage to prevent diseases associated with E. histolytica infection.[17] Common antiinflammatory herbal plants are *Curcuma longa*, *Zingiber officinale*, *Rosmarinus officinalis*, *Borago officinalis*, *Urtica dioica*, *Uncaria tomentosa, Vaccinium myrtillus*, *Olea europaea* and much more. They are believed to be without side effects unlike the chemical counterparts or synthetic anti-inflammatory agents e.g. steroids, nonsteroid anti-inflammatory drugs, and immunosuppressants used for controlling and suppressing inflammatory crisis.[18]

Althaea officinalis

One study was aimed at experimental confirmation of *Althaea officinalis* polysaccharide rhamnogalacturonan antitussive effect and its changes in conditions of allergic inflammation. Rhamnogalacturonan isolated from *Althaea officinalis* mucilage possesses a very high cough suppressive effect in guinea pigs test system, which is shortened in conditions of experimentally induced airways allergic inflammation.[19] One study investigates the potential role of aqueous extract of *Althaea officinalis* flower in lipemia, gastric ulcer, inflammation, and platelet aggregation using the rat model. The aqueous extract of *Althaea officinalis* flower demonstrated potential benefits in lipemia, inflammation, gastric ulcer, and platelet aggregation with no visible adverse effect.[20]

The study aimed to inspect gastro-protective as well as in vitro and in vivo antioxidant potential of *Althaea officinalis* and *Solanum nigrum* extracts on pyloric-ligation/indomethacin-induced gastric-ulceration in rats. Reduction in titratable acidity, gastric mucosal nitric-oxide, antioxidant contents, and protective factors accompanied gastric-ulceration. Additionally, elevation in pro-inflammatory cytokines content and reduction in cystathionine-β-synthase and heme-oxygenase-1 expression was witnessed. Omeprazole, misoprostol, Althaea officinalis, and Solanum nigrum pretreatments fixed blood and tissue biomarkers, thereby protecting them from pyloric-ligation/indomethacin-induced gastric ulceration in rats, which is hopeful for clinical examinations.[21]

Malva sylvestris

The emphasis of the study is to evaluate a natural product and the potential microbicide activity using a dual-chamber infection method. *Malva sylvestris* extracts and fractions were screened for anti-HIV activity by measuring the virus-antibody neutralization. Natural occurring derivatives of M. sylvestris demonstrated to work inhibiting reverse transcriptase enzyme action. M. sylvestris contains highly potential anti-HIV-1 BaL components and may be considered a potential source for new formulations in the development of topical microbicides.[22] The effects of extraction temperature, extraction time, the ratio of water to raw material, and the number of extraction on the extraction yield of crude polysaccharides from the leaves of *Malva sylvestris* (MSLCP) were optimized by statistical analysis using response surface methodology. The response surface methodology (RSM) was used to optimize MSLCP extraction yield by implementing the CCD design. The results demonstrated that MSLCP had strong scavenging activities in vitro on DPPH and hydroxyl radicals. Overall, MSLCP may have potential applications in the medical and food industries.[23]

Cordia latifolia

Recently, one study reported high in vitro antibacterial efficacy of Althaea officinalis, Ziziphus jujuba, *Cordia latifolia,* and Thymus vulgaris out of a total of 21 plants against a wide range of bacteria including MRSA. This study was, therefore, designed to confirm the efficacy of these four herbs against MRSA in an animal model. This is the first report confirming in vivo anti-MRSA potential of C. latifolia and T. vulgaris and highlights the need to explore bioactive constituents of these plants. Moreover, the previously reported in vitro antibacterial efficiency of A. officinalis could not be validated in the current study.[24] The in vitro antibacterial activities of 29 traditional medicinal plants used in respiratory ailments were assessed on multidrug-resistant Gram-positive and Gram-negative bacteria isolated from the sore throat patients and two reference strains. Methanolic extract of 18 plants showed antimicrobial activity against test strains *Cordia latifolia* (ZI = 16-20 mm, MIC: 12.62-62.5 µg/mL) showed significant antibacterial activity. The results obtained from this study provide a scientific rationale for the traditional use of these herbs and laid the basis for future studies to explore novel antimicrobial compounds.[25]

Adhatoda Vasica

COVID-19 pneumonia has been associated with severe acute hypoxia, sepsis-like states, thrombosis, and chronic sequelae including persisting hypoxia and fibrosis. The molecular hypoxia response pathway has been associated with such pathologies and our recent observations on anti-hypoxic and anti-inflammatory effects of whole aqueous extract of *Adhatoda Vasica* (AV) prompted us to explore its effects on relevant preclinical mouse models. Results provide a scientific rationale for this ayurvedic herbal medicine in ameliorating the hypoxia-hyperinflammation features and highlights the repurposing potential of AV in COVID-19-like conditions.[26]

Methanolic extract of *Adhatoda vasica* L. leaves (MEAV) was analyzed by hyphenated gas chromatography-mass spectroscopy for identification and characterization of its bioactive and traditional therapeutic claim. Methanolic extract of *Adhatoda vasica* L. leaves consists of both polar and nonpolar components. GC-MS analysis was used to identify these compounds. The current work validates that the antioxidant activity of the methanolic extract was attributed to the presence of compounds like vitamin E, alkaloid, and terpene.[27]

PubMed and PubChem database literature review on selected 10 plants products including *Coffea Arabica, Curcuma longa, Glycyrrhiza glabra, Zizyphus vulgaris, Sisymbrium irio, Borago officinalis, Althaea officinalis, Malva sylvestris, Cordia Latifolia* and *Adhatoda vasica* indicate that these plant products and their active constituents have significant anti-inflammatory, antioxidant, immunomodulatory and antiviral properties.

Conflicts of Interest

The authors declare that there are no conflicts of interest relevant to this article.

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