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A CRITICAL REVIEW ON PHARMACOLOGICAL AND MECHANICAL PROPERTIES OF DAIDZEIN

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ABSTRACT

Medicinal plants have proved to be of great importance since long back as they are traditionally used to make plant-derived medicines that are a good alternative to synthetic chemicals. Daidzein is one such chemical compound that belongs to the group of isoflavones and is obtained from leguminous plants, especially soy plants. Daidzein is structurally similar to human hormone estrogen due to which is also called a phytoestrogen. Daidzein is an isoflavone compound that is mostly found in glycosylated form in plants while in humans it is found in free form in the bloodstream. It is clinically used in treatment of variety of cancers. It has become quite successful in treating ovarian cancer, breast cancer, and thyroid cancer. Daidzein also possess some exquisite properties such as anti-inflammatory properties, anti-oxidant properties, and neuroprotective properties. In this paper mechanical properties of daidzein are also discussed in which daidzein has been proved as an excellent wood adhesive agent for industrial purpose. Also, daidzein is used as flame retardant and is doing good in dietary supplementations. Daidzein can be important for further pharmaceutical and industrial applications.

Keywords: Anti-cancer; Anti-inflammatory; Daidzein; Flavonoids; Phytoestrogen

1. INTRODUCTION

Medicinal plants have proved to be of great importance since long back as they are traditionally used to make plant-derived medicines that are a good alternative to synthetic chemicals (Wink et al., 2018). There is a huge demand of understanding the pharmacological and biological properties of plant derived components and their potential for the prevention of several pathologies (Romano et al., 2021). Daidzein is such a chemical compound that belongs to the group of isoflavones and is obtained from leguminous plants, especially soy plants (Heinonen et al., 2003). Some of the other sources of daidzein are clovers, bluegrass, chickpeas and other legumes (Iwami et al., 2004). Daidzein is structurally similar to human hormone estrogen due to which is also called a phytoestrogen, but the specificity of the estrogen receptor complex makes daidzein different from estrogen (Sun et al., 2016). Much research has been done to assess the bioactivity of isoflavones using adult humans, rats and mice as models in biomedical research (Soukup et al., 2016). Being one of the isoflavones which are found in soybeans, it has a high range of physiological and pharmacological properties (Dwieki et al., 2009). Daidzein is thought to be highly active in preventing cancers by acting as powerful anti-cancer agents, also check the development of cancer cells by controlling malfunctioning of gene cycle progression (Adjackly et al., 2013). Daidzein has been reported to protect against chest, prostate and colon cancers and shows anti-inflammatory properties, cardioprotective and antioxidant characteristics. Many scientific reports confirmed the convincing effects of daidzein on cerebral ischemic injury and its other vital physiological functions (Choi et al., 2013; Jiao et al., 2021).

2. DAIDZEIN: CHEMICAL NATURE, IT'S METABOLITES AND DERIVATIVES

In chemistry, flavonoids are a class that consist of many non-synthetic compounds with carbon framework C_6-C_3-C_6. Originally isoflavone is a sub-class of iso-flavonoid which belongs to the group of flavonoids. Daidzein is an isoflavone compound that is mostly found in glycosylated form in plants while in humans it is found in free form in the bloodstream (Kim et al., 2008). The chemical name of daidzein is 7,4'-dihydroxyisoflavone and is abundantly available in plants naturally without any artificial aid. Basically, it is present in the form of beta-glycosides in plants (Iwami et al., 2004). The major five metabolites of daidzein are dihydrodaidzein (DHD), tetrahydro daidzein (THD), O-desmethylangolensin, dehydroequol (DE) and equol. The metabolite equol shows 100 times more estrogenic property than parent compound daidzein itself (Kim et al., 2008).

The parent compound isoflavone daidzein (D, pKa_1= 7.47 ± 0.02 and pKa_2 = 9.65 ± 0.07) has three derivative compounds of its own which are three methyl anisole derivatives 7- methyldaidzein (7-Me-D, pKa = 9.89 ± 0.05), 4' methyldaidzein (4'-Me-D, pKa = 7.43 ± 0.03), and 7,4'-dimethyldaidzein (7,4'-diMe -D), is found to slow down the process of oxidation liposomal membranes after a detailed study on it (Liang et al., 2008). From the biotransformation reaction mixture four confined derivatives of daidzein were obtained which are daidzein 7-O-phosphate, daidzein-7-O-β-D-glucoside, daidzene-7-O-β-(6" O-succinyl)- D-glycoside and 4'Ethoxy-daidzein-7-

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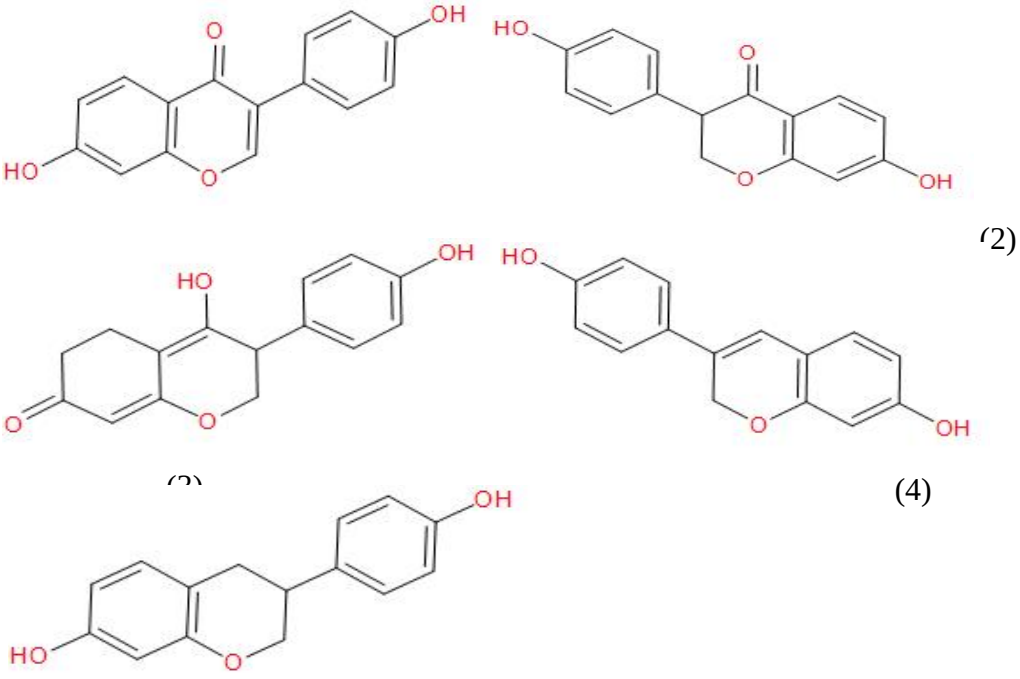
O-β-(6"-O-succinyl)-D- glucoside (Kim et al., 2018). The other study reported four chemical metabolites of daidzein in the forms of 7, 4"-di-O-sulfate, daidzein 7-O-β-D-glucuronide, daidzein 4'-O-sulfate, and daidzein respectively (Yasuda et al., 1994). "-O-methyl-8-hydroxymethyl-daidzein (1) is a new derivative of daidzein which is segregated from Streptomyces sp. 65408 in soyabean powder containing medium (Yang et al., 2013).

Chemical Structure of Daidzein and its metabolite



(1: Daidzein, 2: Dihydrodaidzein (DHD), 3: tetrahydrodaidzein (THD), 4: dehydroequol, 5: equol. Source: Kim et al., 2008)

3. BIOLOGICAL ACTIVITIES

3.1 Anticancer Activity

Daidzein being one of the essential flavonoids showing a high spectrum of pharmacological properties, especially antimicrobial and anticancer activities. As the anti-cancer activity on ovarian cancer is still very less discovered, one study graded anticancer activity of daidzein against a panel of human ovarian cancer cells lines and one normal ovarian cell line and showed that the daidzein exerted good anticancer activity against SKOV3 cells with a half-maximal inhibitory concentration (IC_{50}) of 20 µM (Hua et al., 2018). Equol one of the daidzein metabolite and daidzein itself presented the tendency of checking the growth of mammary tumors in rodents. After a detailed study on it, it was concluded that both daidzein and equol can be used as a core structure to design new drugs for breast cancer therapy and also the intake of daidzein can prevent breast cancer (Liu et al., 2102). In other study anti-breast cancer activity was investigated with Erα and c-erb-2 receptors, and daidzein showed significant effects (Choi et al., 2013). It was reported that daidzein induces programmed cell death (apoptosis) by the process of mitochondrial caspase-dependent cell death pathway in breast cancer cells (Wang et al., 2010) cD-tboc 7-(O)-carboxymethyl daidzein is a novel derivative of daidzein which was created by a laboratory experiment for checking the growth human thyroid cancer cells, the results suggested that it can act as a favorable agent in thyroid carcinoma either alone or in combination with existing cytotoxic drugs (Somjen et al., 2011). Daidzein plays a significant role in anti-prostate cancer activities both in-vitro and in-vivo. S-equol, a derivative of daidzein targets Akt/FOXO3a for the survival of prostate cancer, in the progression of cell cycle and apoptosis (Guo et al., 2016).

3.2 Anti-Inflammatory Activity

One survey was conducted to know the actual activity (structurally) of isoflavone daidzein and also to modify it by incorporating the derivatives of daidzein namely sulfonic acid ester derivative (2-4). It was concluded that anti-inflammatory activity was confirmed in all three compounds. The study also recommended that daidzein sulfonic acid esterification at 4'- and/or 7- position can potentially enhanced the several biological activities including physiochemical and pharmacological properties and also enhanced the cellular uptake or process of absorption (Peng et al., 2017). One research was conducted to identify whether daidzein could regulate the production inflammatory mediators in macrophages stimulated with lipopolysaccharide (LPS) from Prevotella intermedia. Based on the research it was interpreted that daidzein can act as an encouraging representative for the treatment

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of inflammatory periodontal disease. Also, advance research is required for better knowledge of daidzein as novel therapeutic agent in treating periodontal disease in animal models (Choi et al., 2012).

3.3 Anti-Oxidant Activity

With a defined protocol being followed in-vitro oxidative activity assay was accompanied in which the cells were stimulated with 500 µL Hydrogen peroxide (final concentration 0.04 Mm). Cells stimulated with H_2O_2 were incubated for 6 hours prior to the WST-1 assay, after which the supernatants of cell culture were assembled and stored at 80°C for subsequent ELISA experiments, it was concluded that the daidzein-7- benzene sulfonate showed strong anti-oxidative effect at 100 micrometers (Peng et al., 2017). Based on one study the potential of daidzein along with its metabolites was checked as an antioxidant agent and it was concluded that antioxidant activity of daidzein was weaker than that of its metabolites and also the anti-oxidant activity of daidzein was stronger than that of daidzin (Choi et al., 2014). The antioxidant activities of O-DMA, equol, daidzein, and daidzin were in descending order i.e., daidzein > equol > O-DMO > daidzin for catalase and equol > O-DMO > daidzein > daidzin for total SOD. Phytochemical methods such as cisplatin- induced lipid peroxidation, protein nitration and NOX_2 mRNA with the help of daidzein was reported (Meng et al., 2017). Baechler and Co-workers in their study hypothesized that oxidative metabolism of daidzein may induce the formation of hydroxylated metabolites and genotoxic properties were found to be obtained by oxidative metabolism of daidzein along with involvement of topoisomerase II which might play role in it (Baechler et al., 2014).

3.4 Neuroprotective Activities

Daidzein which is mainly obtained from soy plants and also called phytoestrogen is clinically treated and used. With the knowledge of neuroprotective properties of estrogen, it is believed that the extracts of daidzein and soyabean can improve memory power and exhibit neuroprotective roles in brain. In a recent study, baicalein and daidzein have found to be helpful in prevention of Aβ-induced neuronal death acting as prominent two effectors in activating estrogen-mediated pathway (Choi et.al 2013). Daidzein validates hypothesis that it reveals neuroprotective effects on cerebral ischemia. Daidzein is found to reduce oxygen free radical production and shows neuroprotective effects on ischemic brain (Aras et al., 2015). By using membrane-based model of obesity related inflammation in a study it was discovered that daidzein moderated neuroprotection in hypothalamic neurons. Several other biological activities like cell death, proinflammatory processes, oxidative stress and apoptosis is also controlled and checked by daidzein by protecting hfHypo GnRH cells (Morelli et al., 2020).

4. MECHANICAL PROPERTIES

Daidzein is a 100% bio-based wood adhesive. Daidzein and epichlorohydrin was mixed with soy protein to make adhesives. The yield obtained was 93.47% in preparation. The crosslink agent was then systematically mixed with the soy protein isolate adhesive system along with the safety data sheet, double cross linked network structure was formed by hot pressing process by binding with protein molecules. This structure helps in achieving desirable properties, water resistance, rigidness and thermal stability (Zhang et al., 2020).

Benzoxazine resin (Dz-f) is a biobased benzoxazine resin which is obtained from daidzein shows outstanding thermal properties (Dai et al., 2018). In a research work, aromatic/aliphatic diamine, and paraformaldehyde was synthesized from isoflavone daidzein, the obtained results showed excellent thermal stability and low flammability, with a Tg value greater than 400 °C, and a heat release capacity (HRC) value lower than 30 J/(gK). Two types of main chain benzoxazines polymer's thermal stability and flame retardant properties of the resulting polybenzoxazines were investigated using TGA and microscale combustion calorimeter (MCC) and the results obtained were desirable (Han et al., 2019).

5. OTHER PROPERTIES

Daidzein along with diphenyl phosphonyl chloride has drawn up an organophosphorus flame retardant (DPOD) which is used to improve the flammability of epoxy (EP) resin. The chemical structure of daidzein allows easy reaction with flame retardant groups and is advantageous for the formation of char at high temperature. A flame retardant which can work in both the gas phase and the condensed phase may be exceptionally effective (Li et al., 2019).

Daidzein has also shown significant improvement in dietary supplementation. It helps in improving production of eggs. One study revealed that daidzein -CH mixture given along with supplementing diets can enhance the egg laying performance by increasing plasma antioxidant activity, luteinizing hormone levels, and mineral content (Xiao et al., 2019).

An electrode sensor was prepared by directly incorporating ZrOCl2 into graphite powder after with an electrochemical treatment and this sensor exhibited showed sensitive voltametric sensing for daidzein. This sensor was applicated in identification of daidzein in Pueraria, pharmaceutical preparations and human uric sample with convincing results (Wang et al., 2015).

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6. CONCLUSION

Daidzein is a chemical component derived from soy plants and legumes and is structurally similar to human hormone estrogen. It is clinically used in treatment of variety of cancers. It has become quite successful in treating ovarian cancer, breast cancer, and thyroid cancer. Daidzein also possess some exquisite properties such as anti-inflammatory properties, anti-oxidant properties, and neuroprotective properties. In this paper mechanical properties of daidzein are also discussed in which daidzein has been proved as an excellent wood adhesive agent for industrial purpose. Also, daidzein is used as flame retardant and is doing good in dietary supplementations. Daidzein can be important for further pharmaceutical and industrial application. A lot of research is currently underway on the daidzein.

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