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PUERARIA LOBATA PLANT AND ITS BIOACTIVE METABOLITES: CHEMISTRY, PHARMACOLOGY, AND THERAPEUTIC POTENTIAL

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ABSTRACT
Chapters in the review article provide a deep dive into isoflavonoids and this triterpenoid puerarin reviewing chemical structures, properties, oral bioavailability and pharmacological effects. Puerarin is a traditional Chinese herbal medicine derived from the "Gegen" plant, which shows anticancer and anti-inflammatory activity, but its clinical application has been greatly hindered by extremely low bioavailability attributed to glucopyranose. Daidzein is another phytoestrogen and a bioactive compound with various metabolites that have estrogen-like actions which has been used in bio-based wood adhesives as well as flame retardants. Genistein: Found in soy products, it exerts estrogenic activity and has antioxidant properties, antidiabetic effects, and anticarcinogenic properties, but clinical use is limited by its poor bioavailability. Formononetin, belonging to the Fabaceae family, exhibits anti-inflammatory, antidiabetic and antimicrobial properties. Lupeol is a natural triterpanic compound derived from several plant species and known for its antimetastatic, antitumor and anti-inflammatory activities. Coumestrol is a phytoestrogen found in legumes that has neuroprotective and immunomodulatory properties. Researchers have proposed it to be used in the treatment of different psychiatric and neurological disorders. The article also describes their chemical structures backed by various Anticancer properties studies showed their all molecular structure.

KEYWORDS: Traditional Chinese medicine monomer, phytochemical constituents, Pharmacological effects.

Puerarin

High concentrations of isoflavonoids are found in the species Pueraria.[1] Gegen is a traditional Chinese herbal treatment that has been used to extract puerarin (PR), an isoflavonoid. 7-hydroxy-3-(4-hydroxyphenyl)-8-β-D-glucopyranosylPuerarin is chemically known as 4′, 7-bihydroxy-8-β-D-glucoisoflavone or -4 H-1-benzopyran-4-one. Molecule formula: C21H20O9.[2]

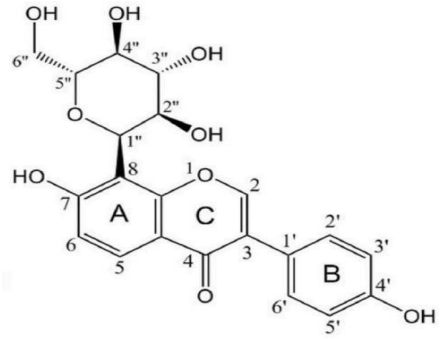

Fig.1: The chemical structure of puerarin.[3]

Its limited bioavailability is caused by the glucopyranose group at position 8, which forms a steric barrier that keeps puerarin from passing through the intestinal mucosa.

Puerarin's poor absorption through the mouth led to the successful development of injection, which is currently a commonly used dosage form in clinical practice.[4] Solid self- microemulsion capsules, solid dispersions of puerarin phospholipid complexes, and Multiabsorption enhancer-puerarin tablets are some of the modified oral formulations of puerarin that have been created that are easily absorbed.[5]

Pharmacological Effects

Puerarin has a range of anticancer and, including anti-inflammatory and anti-breast cancer, anti-prostate cancer, inhibition of other cancers, anti-cardiovascular diseases, anti-osteoporosis, anti-aging, anti-inflammatory, and neuroprotective properties.[6]

Daidzein

The class of chemicals known as flavonoids is made up of numerous non-synthetic molecules with a C6–C3 carbon structure. Isoflavones are originally a subclass of iso-flavonoids, which are flavonoid compounds.[7] An isoflavone called daidzein is primarily present in glycosylated form in plants, but it can also be detected in free form in the bloodstream of people. Daidzein's chemical name is 7,4'-dihydroxyisoflavone. Dihydrodaidzein (DHD), tetrahydrodaidzein (THD), O-desmethylangolensin, dehydroequol (DE), and equol are the five main metabolites of daidzein. More oestrogenic properties are displayed by the metabolite equol than by the parent molecule daidzein.[8]

Membranes of isoflavones are the primary compound. Daidzene, Daidzein-7-O-β-D-glucoside, and Daidzein 7-O phosphate7'O-β-(6'' O-succinyl)-D-glucoside and 4'Ethoxy-daidzein-7O-β-(6'' O-succinyl)-D-glucoside).The other study revealed four chemical metabolites of daidzein in the forms of 7, 4”-di-O-sulfate, daidzein 7-O-β-D-glucuronide daidzein.[9-11]

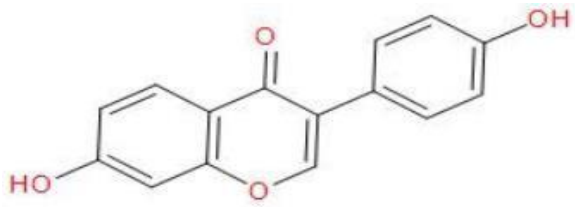

Fig. 2: Chemical Structure of Daidzein.[12]

Mechanical properties of Daidzein

A 100% biobased wood glue is called Daidzein. Adhesives were created by combining soy protein with daizenein and epichlorohydrin.[13] In preparation, a yield of 93.47% was achieved. The crosslink agent was then methodically combined with the safety data sheet and the soy protein isolate adhesive system.[14] By connecting with protein molecules during the hot pressing process, a double cross-linked network structure was created.[15]

Other properties of Daidzein

An organophosphorus flame retardant (DPOD), created by daizenzin and diphenyl phosphonyl chloride, is used to increase the flammability of epoxy (EP) resin.[16] Daidzein's chemical structure facilitates the development of char at high temperatures and makes it easier for it to react with flame retardant groups.[17]

Pharmacological Effects

Daidzein has several other biological properties that are not related to the ER, including anti-inflammatory and anti-cancer properties, inhibition of oxidative damage, and nerve and skin protection.[18] These advantageous benefits are mostly caused by immune response control, oxygen free radical scavenging, proliferation inhibition, and other mechanisms.[19] On the other hand, when daizezin is displayed in the bound form.[20]

Genistein

The Fabaceae family includes the widely distributed isoflavone genistein, which was initially isolated from Dyer's Genista tinctoria L., a broom plant.[21] Mammalian genistein performs estrogen-like activities as an isoflavone. Genistein primarily comes from soy products.

Originally from Asia, soy is part of the legume species, its grains growing in pods. All we use for food are the berries; other parts of the plant, such as the white or purple parts, are used in industry and medicine.[22]

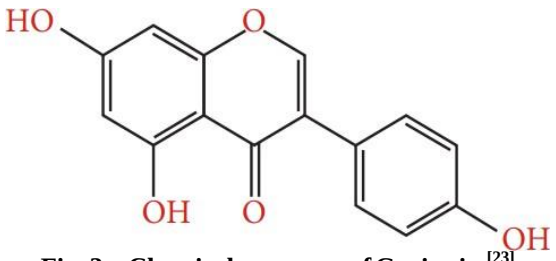

Fig. 3: Chemical structure of Genistein.[23]

A member of the aglycone family, genistein is one of the most well-known and studied isoflavones. Isoflavones are almost exclusively found in naturally occurring glycosylated forms; they are only made available in physiologically active forms, known as aglycones, through food processing.[24]

Isoflavones operate similarly to oestrogen in mammals. Genistein (5,7-dihydroxy-3-(4-hydroxyphenyl)chromen-4-one) exhibits estrogen-like activity primarily because of carbons 4 and 7 on the phenol rings. These carbons are structurally and functionally similar to the phenol groups on E2, allowing them to bind to both the α and β isoforms of the oestrogen receptor equally.[25] 4′,5,7-trihydroxyisoflavone or 5,7-dihydroxy-3-(4-hydroxyphenyl) is the chemical name.1-benzopyran-4-one, or -4H-1 C15H19O4 is the chemical formula. Weight in grammes per mole (g/mol): 270.24; IUPAC name: 4′,5,7-Trihydroxyisoflavone.[26]

Bioavailability

There are two ways to estimate the oral bioavailability of genistein: the first is absolute bioavailability, which is determined by comparing the AUCoral of plasma and urine to the AUCiv after dosage adjustment (traditional

pharmacokinetic definition). The AUCoral of urine or plasma can be counted to estimate the oral bioavailability of genistein.[27] The percentage recovery based on the administered dose is then obtained. Low oral bioavailability of genistein was revealed by pharmacokinetic studies. Concurrently, investigations into the bioavailability of genistein on portal vein plasma levels revealed that genistein's aglycon has a higher bioavailability than its glycoside portion. The glycosidic form of genistein is partially absorbed.[28]

Pharmacological Activities of Genistein

Genistein program, Antioxidant Activity: Effects on Lipid Metabolism, Depression, Neurodegenerative Diseases, Anticancer and Cytotoxic Activity, Antibacterial and Antiviral Activity, Anti-diabetic and Its Effects. Anti-osteoporosis and anti-cardiovascular diseases.[29-31]

Formononetin

Formononetin, an isoflavone that occurs naturally and is a member of the Fabaceae family, is present in many dietary products at low amounts.[32] Biochanin B is the chemical name of formononetin, and 7-Hydroxy-4'-methoxyisoflavone, or 7-hydroxy-3-(4-methoxyphenyl)-4H-chromen-4-one, is its IUPAC designation. The chemical formula for it is C16H12O4. 268.26408 g/mol is its molecular weight.[33]

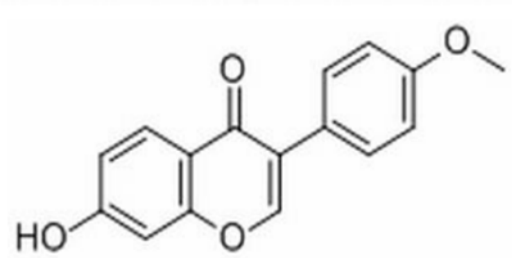

Fig. 4: chemical structure of Formononetin.[34]

Formononetin, whose various pharmacological effects have been proven. (Vaya and others, Through an increase in AP-1 DNA binding activity, formononetin upregulates the production of interleukin-4 in activated T cells. Formononetin exhibits anti-inflammatory properties by inhibiting the release of arachidonic acid in HT-29 human colon cancer cell lines. (Jun and colleagues, 2005).

Formononetin lowers blood pressure and central arterial stiffness, which lowers the risk of cardiovascular disease.[35] By turning on the receptors for PPARα and PPAR-γ Formononetin controls lipid metabolism as a strong antidiabetic drug. Mononetin showed analgesic efficacy and promoted osteoblast growth in a mouse model of abdominal constriction produced by acetic acid. Similar to AST, formononetin elicited growth inhibition and enhanced caspase-dependent apoptosis in human colon cancer cells. inhibition of proteins known to be anti-apoptotic Several plants belonging to the third-largest family of land plants, the "Fabaceae," or bean family, have been reported to contain formononetin. All 250 species in the genus Trifolium (Fabaceae) have been shown to be rich sources of formononetin. In addition to this family, formononetin is also present in diferent plants including Trifolium pratense Glycine max. Formononetin is extracted from diferent plants such as Dalbergia odorifera in which Formononetin along with other compounds.[36-40]

Pharmacological effects of Formononetin

This compound showed antiallergic and anti-inflammatory activities. Formononetin together with other known compounds acts as active inhibitor of EV-A71 infection Brazilian Red propolis extract containing isoflavonoids such as Formononetin exhibits anti-inflammatory potential in a rat model of inflammation Isoflavones such as Formononetin isolated from soy bean possess antimicrobial and antioxidant activities with IC50 values from 10.6 to 22.6 g/mL that a methoxy Isoflavone, Formononetin.[41-45]

Lupeol

Lup-20-en-3-ol generally known as lupeol clerodol, fagarsterol and lupenol, is mainly identified by its 1 H and 13C NMR spectral.[46] Scientific Name of Lupeol - 3-lup-20(29)-en-3-ol Rings present 6 member rings- 4 (total number), contain chair conformation 5 member rings- 1 (total number), contain envelop Three -dimensional structure. That is, a kind of terpen develops with plants.[47] The chemical formula of lupeol is C30H50O and its melting point is 215-216°C. Its molecular formula is 426.7174 g/mol. The structure of lupeol contains 10 asymmetric centers, making the synthesis of lupeol a stereochemical challenge.[48] Although there have been several attempts to synthesize lupeol by various routes, lupeol tends to be obtained from natural sources, such as plants rich in lupeol, such as Crataeva nurbara and birch bark, or from industrial waste from cork processing.[49] It is made up of 12 anthraquinones, phenolic compounds that were once used as enemas. It contains minerals such as Ca, Cr, Cu, Mg, Mn, Se, K, Na, Zn etc.[50] It contains monosaccharides and polysaccharides. It contains cholesterol, kempsterol, β-sitosterol, lupeol and other plant hormones.[51]

Characteristics of Lupeol- Lupeol extracted by esterification method. To obtain lupeol esters, the following carboxylic acids and their anhydrides were used as acylating agents: acetate, propionate, isonicotinate, succinate and acetylsalicylate.

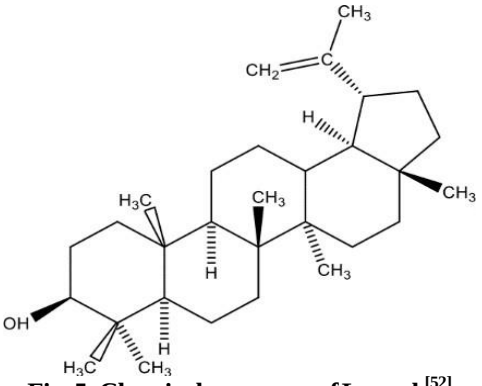

Fig. 5: Chemical structure of Lupeol.[52]

Pharmacological activity of lupeol

Lupeol exhibits the following functions: antimetastatic, antitumor, antileukemic, antihyperglycemic, anti-inflammatory, antidiabetic, cardioprotective, skin protective, antimicrobial, antiviral, nephroprotective, antiprotozoal.[53-55]

Coumestrol

Cuemes are polycyclic aromatic secondary metabolites containing the fragment of the kumstan, which consists of a benzovshososh merged with Chims-2-Oo-ono-ono-ono-benoxosol [3,2-c] Chman-6-One, heterocycrique trivial name Coumestan, four ringtone . The system was proposed by Mentzer, which has a systematic name for 6 hours for the skeletal structure of the benzofuro-one chainsaw and was adopted by chemical summaries. The presence of two free hydroxyl groups was indicated by the formation of diacexil and dimoxic production, the empirical formula, C15H8O5 differs from a typical flavonoid in the absence of two hydrogen atoms. Fusion studies yielded only resorcinol and f3-resorcylic acid, providing insight into the number and position of hydroxyl groups on both rings.[56-59] Kestrol was originally isolated from the Alphafa. Later, the plants of this Kumestan were found in various legumes, soy, buds, clover, and spinach. Coumestrol has been shown to have a broad range of biological effects, including neuroprotection and immunomodulation. Coumestrol, a phytoestrogen that can be extracted from certain plants such as Ladino clover and alfalfa, belongs to a group of biological chemicals called coumestans. It is well known to exert certain effects on reproduction via the beta-type estrogen receptor.[61] The range of pharmacological properties of coumestrol is not limited to the genitals, although.

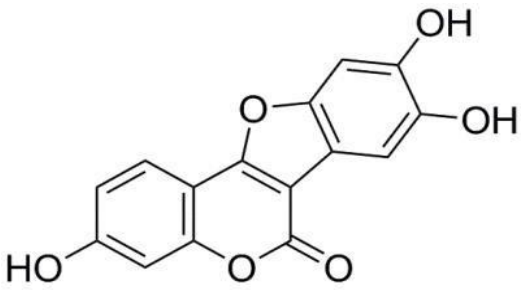

Fig. 6: Chemical structure of Coumestrol.[62]

Pharmacological aspects of the Coumestrol

Phytoestrogens reduce certain psychiatric and neurological problems such as Alzheimer's disease, cerebral hypoxia-ischemia, anxiety, depression, and certain types of cognitive impairment, and more effectively treat a variety of diseases such as osteoporosis, obesity, inflammation, photoaging of the skin, autoimmune thyroiditis, cancer, and certain cardiovascular diseases.[63-66]

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