Chamomile

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Matricaria chamomilla L. (MC) and *Chamaemelum nobile* (L.) All. (CN) are two varieties of Chamomile. These herbs have been used for thousands of years in Greece, Rome and ancient Egypt. Chamomile has been used for the treatment of stomach problems, cramps, dermatitis, and minor infections.

Matricaria chamomilia L. Chamaemelum nobile (L.) all. chamomile

1. Introduction

Traditional Chinese medicine (TCM) has been used for a long time in China and recorded for more than 5000 years. Numerous herbs have been used in TCM [1]. This field is becoming an integral part of various traditional medicine and modern medicine systems globally. In modern medicine, it is primarily used to prevent various diseases. Therefore, TCM is gaining popularity worldwide and supports human health greatly [2].

Chamomile is an annual or perennial plant belonging to the family Asteraceae. The plant improves the appetite and relieves painful swellings and sweating [3]. Chamomile is native to temperate regions of Asia and Europe, and cultivated worldwide for its high medicinal, cosmetics and food value [4]. It has been used for thousands of years in Greece, Rome and ancient Egypt. In China, the detailed use of this plant was first recorded in Uyghur medicine. Veteran doctors of TCM believe that preparations containing chamomile have a calming effect. In addition, the plant is also used in other traditional, homoeopathic and Unani preparations [5][6]. There are two main varieties of chamomile: *Matricaria chamomilia* L. (MC) and *Anthemis nobilis* (L.) All. (CN). *Matricaria chamomilia* L. belongs to the genus *Matricaria*. It is an annual plant, and the flowering period is from May to July in China. *Chamaemelum nobile* (L.) All. is a perennial plant of the genus *Chamaemelum*. The flowering period is from April to May in China [7][8]. *Matricaria chamomilia* L. is relatively common and has been researched and used widely. At present, 26 countries around the world have included this plant in their pharmacopoeia. Chamomile flower heads are commonly used for medicinal purposes [9]. Chamomile contains flavonoids, coumarins, volatile oils, terpenes, sterols, organic acids, and polysaccharides, among other compounds. Having a wide array of compounds, chamomile exhibits various pharmacological activities such as anticancer, anti-infective, anti-inflammatory, antioxidant, hypoglycaemic, hypotensive, hypolipidaemic, antiallergic, antidepressant, and neuroprotective effects, and others [3][4][5][6][7][8].

Pictures of two species of chamomile from the Global Biodiversity Information Facility "https://www.gbif.org (accessed on 16 November 2022)" are shown in **Figure 1**.

Figure 1. Two species of Chamomilla: *Matricaria chamomilia* L. (**a**), *Chamaemelum nobile* (L.) All. (**b**).

2. Pharmacological Activities

2.1. Anticancer Activity

Glioma is one of the common intracranial malignant tumors with high incidence, rapid growth, high recurrence rate, high mortality and poor prognosis. α-Bisabolol, a fat soluble sesquiterpene compound that is widely found in Chamomile essential oil, has been proven to possess the potential to affect glioma. Yan et al. tested the effect of α-bisabolol on human brain glioblastoma cells (U251 and U87) using the scratch assay. Its effect on migration and invasion was investigated. Protein expression studies have been conducted using Western blot. α-Bisabolol inhibited gliobla stoma cell migration and invasion by down regulating central mucoepidermoid tumor (c-Met) [10]. α-Bisabolol oxide A and apigenin-7-β-D-glucoside, obtained from chamomile flowers and stems, are reported to inhibit the migration of Caco-2 colon cancer cells and deactivate the vascular epidemal growth factor receptor-2 (VEGFR2) angiogenic enzymes [11]. Apigenin is a flavonoid component of this plant, which also shows a certain anticancer effect on the liver cancer cells (Hep G2) and leukaemia cells (HL-60) [12]. Additionally, Srivastava et al. confirmed that apigenin 7-O-glycoside obtained from chamomile extract had a good anticancer effect, but its effect was lower than that of apigenin [13].

In vitro studies confirmed the antiproliferative effect of this plant on cervical cancer cells (HeLa) [14]. The anticancer activity is mediated through the Wnt pathway in colon tissue, down-regulating the expression levels of factors such as wingless integration-5A (Wnt5A), β-catenin, transfer cell factor 4 (Tcf4), and up-regulating the expression levels antigen presenting cell (APC) and GSK-3β [15]. Hydroalcoholic extracts of chamomile (dose-and time-dependent) have been reported to increase apoptosis and necrosis, decrease cell proliferation or migration, colonization, invasion and attachment in Michigan cancer foundation-7 (MCF-7) and MDA-MB-468 cell lines [16]. Chamomile fermented with *Lactobacillus plantarum* for 72 h showed selective cytotoxicity on cancer cells compared to normal cells (medical research council cell strain 5 (MRC-5)) [17].

2.2. Anti-Infective Activity

Chamomile volatile oil has shown an anti-infective effect on the growth of fungi and bacteria [18]. Furthermore, it effectively reduces the protease in mites and can be used to treat urticaria [19]. Mean corpsular hemoglobin-ampicillin 1 (MCh-AMP1), a natural peptide from the plant, has broad-spectrum antifungal activity against human pathogenic moulds and yeasts. It kills *Candida albicans* by increasing cell membrane permeability and inducing reactive oxygen species (ROS) production [20]. Shikov et al. reported that the minimun inhibitory concentration 90 (MIC90) and MIC50 of chamomile extract against *Helicobacter pylori* were 125 and 62.5 mg/mL, respectively. In addition, this extract controls the production of urease via modulating the morphology of *H. pylori* and fermentation capacity [21]. At present, many mouthwashes and sprays made with chamomile are used for oral bacteriostasis in clinical products, such as the White Gold Medal Compositae essence Product [22].

2.3. Anti-Inflammatory Activity

The flavonoids in chamomile are reported to be responsible for its anti-inflammatory effects. The possible mechanism involves the suppression of nuclear factor kappa beta (NF-κB)-driven transcription [23]. Yuan et al. reported the potent anti-inflammatory activity of Chamomile volatile oil in animal models mediated by inhibiting the production of inflammatory mediators (tumor necrosis factor alpha (TNF-α) and interleukin-1β (IL-1β)) [24]. Because of this activity, chamomile is often used to treat inflammatory diseases such as mammitis, colitis, dermatitis, cystitis, and conjunctivitis [25]. Chamomile Jinshui, an essential oil mainly composed of Chamomile, can effectively relieve prickly heat in children caused by sweat gathering around sweat glands in summer [26].

2.4. Antithrombotic Activity

Cardiovascular diseases (CVD) are one of the leading causes of death worldwide. Chamomile extract exhibits antithrombotic activity by prolonging coagulation and hemostasis time [27]. Luteolin in this plant prevents the development of oxidative stress in adenosine diphosphate (ADP)-induced carotid artery thrombosis in rats [28]. Bijak et al. reported that polyphenol-polysaccharide conjugate obtained from chamomile exerts an antithrombotic effect by reducing platelet aggregation [29]. Bas et al. discovered that half-maximal inhibitory concentrations (IC_{50}) of water and butanol extracts on angiotensin-converting enzyme (ACE) were 1.292 mg/mL and 0.353 mg/mL, respectively [30]. All of the above findings further validate the antithrombotic activity of chamomile.

2.5. Antioxidant Activity

Volatile oil [31], polysaccharides [32][33] and total flavonoids [34][35] of Chamomile have been confirmed to scavenge 1,1-diphenyl-2-picrylhydrazyl (DPPH) and hydroxyl free radicals. The antioxidant effect is dose-dependent [36]. In addition, chamomile ethanol extract increases the activities of superoxide dismutase (SOD) and glutathione peroxidase (GSH-PX) and reduces the malondialdehyde (MDA) content in mice [37]. These findings provide a scientific basis for the antioxidant effect of Chamomile.

2.6. Hypoglycaemic Activity

Chamomile extract reduces fasting blood glucose levels in diabetic mice [37][38] and normal mice and improves glucose tolerance [39]. In addition, the extract antagonizes the effect of exogenous glucose [27]. Yang et al. reported the hypoglycaemic effect of total flavonoids in this plant occurs by reducing fibrinogen (FBG), glycated haemoglobin, glucose tolerance and glycated serum protein (GSP) levels in diabetic mice, and promoting glucose tolerance and insulin secretion [40]. Cemek et al. investigated the hypoglycemic effect of chamomile extract in streptozotocin (STZ)-diabetic rats. The results showed that it protected islet cells and reduced the oxidative stress associated with hyperglycaemia [41].

2.7. Antihypertensive Activity

Studies have found an antihypertensive activity of chamomile extract in essential hypertensive rats [42]. At the same time, another study found that chamomile extract did not affect the systolic blood pressure (SBP) and diastolic blood pressure (DBP) in normotensive rats, suggesting it has no toxic side effects in normal blood pressure regulation [43]. Luo et al. reported that the antihypertensive activity of chamomile extract in N-omega-nitro-L-arginine (L-NNA)-induced hypertensive rats is mediated by reducing angiotension Ⅱ (Ang Ⅱ) content and oxidative stress, and increasing SOD content [44].

2.8. Hypolipidaemic Activity

Hyperlipidaemia (HLP) refers to a metabolic disorder syndrome in which lipid components in plasma are abnormally dysregulated (increased serum total cholesterol (TC), triglyceride (TG), and low-density lipoprotein cholesterol (LDL-C), with decreased high-density lipoprotein cholesterol (HDL-C)). Chamomile is an effective blood lipid-lowering herb. Lan et al. reported that a chamomile alcohol extract played a role in lowering lipids, reducing TC, TG and LDL-C values and elevating HDL-C values in the blood of experimental hyperlipidemic rats [45]. A compound in fuzhuan tea, a popular compound tea containing chamomile with a mellow taste and no toxic side effects, can also treat HLP by regulating the above various sterol indicators [46].

2.9. Antiallergy Activity

As a conventional medicine, chamomile is frequently used to relieve various allergic symptoms. Antiallergic tea, as an example, has positive anti-allergy activity and cosmetology when it is drunk for a long time [47]. The antiallergic activity of chamomile aqueous extract (1.0 mg/mL) was reported by measuring the β-hexosaminidase (β-Hex) release in rat basophil leukemia (RBL-2H3) cells. This was suggested to inhibit the β-Hex release by 21.42% [48]. A chamomile methanol extract could restrain compound 48/80-induced allergic reactions. The effect was dose-dependent and mediated via decreased histamine release and NO levels from mast cells [49].

2.10. Antidepressant Activity

Essential oil aromatherapy is considered an alternative treatment for depression. Chamomile is an excellent reliever when patients with depression have physical and psychological discomfort [8]. Chamomile tea made from chamomile flower heads can effectively relieve depressive symptoms and the sleep status of postpartum women,

which provides a new idea for treatment of depression [50]. Some pharmacological experiments have suggested the antidepressant activity of Chamomile [51]. For example, α-pinene contained in this plant elevated protein expression related to oxidative phosphorylation and mRNA expression of parvalbumin in rat brain, as determined by isobaric tag for relative and absolute quantitation (iTRAQ) and polymerase chain reaction (PCR) analysis [52].

2.11. Organoprotective Effect

Chamomile has protective effects on organs such as the liver, lung, kidney, and stomach, among others.

2.11.1. Hepatoprotective and Pulmoprotective Effect

Chamomile flavonoids ameliorated mouse liver injury by restoring biochemical and molecular parameters in 1,2-Dimethyl hydrazine (DMH)-induced mice [53]. Zhang et al. ascertained that apigenin in this plant could treat APAP-induced liver injury by activating the adenosine monophosphate-activated protein kinase/GSK-3β (AMPK/GSK-3β) signaling pathway, promoting carnitine palmitoyl transferase 1A (CPT1A) activity and activating the nuclear factor erythroid 2-related factor 2 (Nrf2) antioxidant pathway [54]. Additionally, chamomile increases the total antioxidant capacity (TAC) and tissue transglutaminase (tTG) content in liver tissue, protecting against oxidative liver injury from paraquat (PQ) poisoning [55]. On the other hand, its extract protects oxidative lung damage from PQ poisoning, mainly by improving lipid peroxidation (LPO), SOD, glutathione peroxidase (GPx), and increasing the transporter associated with antigen processing (TAP) in plasma and lung tissue [56].

2.11.2. Nephroprotective Effect

According to records in the “Baidu Yi Medicine Book”, chamomile is able to resolve the threat posed by kidney stones [7]. Modern pharmacological studies confirm this plant is an alternative therapy for gastric protection. For example, Salama et al. evaluated the protective effect of chamomile against cisplatin nephrotoxicity by intraperitoneal injection in rats. The study demonstrated that it reduces oxidative stress markers, corrects hypocalcemia caused by cisplatin nephrotoxicity, and inhibits glutamyltransferase activity [57]. In addition, its extract also inhibits phenomena such as glomerular fibrosis, improves renal tissue structure, and protects against renal tissue damage resulting from hypertension [44].

2.11.3. Gastroprotective Effect

Chamomile is a promising gastroprotective herb to deal with stomach spasm, flatulence, stomachache, and decreased gastric secretion [58]. Its extract has shown antiulcer and antioxidant effects in ethanol-induced gastric mucosal injury in rats. Gastroprotective effects are mediated by reducing MDA levels, increasing GSH levels [59], protecting gastric sulfhydryl groups and the opposing effects of intracellular mediators such as free iron, hydrogen peroxide, and calcium [60].

2.12. Genitoprotective Effect

Chamomile extract improves reproductive function in polycystic ovary syndrome (PCOS) rats. Chamomile reduced the uterine and insulin resistance index, regulated sex hormones, leptin and blood lipids, and decreased inflammatory cells [39]. In addition, the interaction of chamomile with the GABA system can regulate luteinizing hormone (LH) secretion and increase dominant follicles for improving reproductive function in rats [61]. Soltani et al. performed surgical experiments on rats and treated the experimental group with chamomile extract. Histological characterization showed that the extract protected the testicular tissue from torsion/detorsion-induced damage by reducing MDA levels and inhibiting superoxide production [62]. Afrigan et al. injected formaldehyde and chamomile extract intraperitoneally into male Wistar rats to probe the hormonal status and sperm parameters of testicular tissue. It was found that this extract reduced the adverse effects of formaldehyde on the reproductive system in male rats [63].

2.13. Neuroprotective Effect

Chamomile has an excellent neuroprotective effect. Its extract restores scopolamine-decreased brain-derived neurotrophic factor (BDNF) expression, increases IL1β, and modulates cholinergic activity in the rat hippocampus [64]. It has been reported that a chamomile ethanol extract improves formaldehyde-induced memory impairment by reducing cell death and MDA content in the hippocampus, and increasing total antioxidant capacity [65]. Furthermore, Lim et al. found that apigenin in this plant inhibits H2O2-induced hippocampal cell (HT22) death [66]. Khan et al. reported the anti-Parkinson activity of chamomile extract by establishing an experimental animal model with chlorpromazine (CPZ). The extract showed vascular proliferation and increased the number of reactive glial cells [67].

2.14. Analgesic Activity

As early as hundreds of years ago, Chamomile was used as an analgesic remedy to relieve a variety of pains, such as arthralgia, stomach cramps, and neuralgia [68]. Nowadays, chamomile oil gel has been authenticated as an analgesic by reducing migraine pain without aura [69]. Saghafi et al. also reported the breast pain-relieving effect of chamomile (treated for 8 weeks) in patients using a visual analogue scale (VAS) and a breast pain scale (BPC) [70].

2.15. Antidiarrheal and Antispasmodic Activity

Chamomile is widely used in traditional Tunisian medicine and TCM against diarrhea and spasticity. In Germany, the extract of this plant is effective in treating children's acute diarrhea by reducing symptoms and shortening the duration of disease [71]. Mehmood et al. reported the antidiarrheal and antispasmodic effects of chamomile using isolated rabbit jejunum. The chamomile extract activates K^+ channels and reduces Ca^{2+} antagonism [72]. Hichem Sebai reported the beneficial effects of the extract in castor oil-induced diarrhea, which decreased MDA levels and antioxidant enzyme activity [73]. In addition, apigenin and apiin in Chamomile have a strong antispasmodic effect on smooth muscle [74].

2.16. Cosmetic Activity

Chamomile is useful in repairing sensitive skin, eliminating acne, and improving skin dehydration. It whitens the skin by inhibiting tyrosinase activity [75]. Therefore, it can be used as an ingredient in skincare products [74]. Ointments, creams and lotions containing chamomile active ingredients are used for the treatment of various skin infections and rashes in Europe and other places [76]. Chamomile Natural Milk Hand Soap, is widely popular for decontamination and sterilization, and can effectively moisturize the skin, enhance elasticity, and calm broken micro-blood vessels [77].

2.17. Other Activities

Chamomile alleviates muscle atrophy by suppressing muscle ring finger-1 (MuRF1) and increasing mitochondrial transcription factor A (TFAM), MyoD and myogenin-1 genes [78]. It relieves stiffness and pain in people suffering from knee osteoarthritis [79]. It also relieves general anxiety [80][81], with efficacy equivalent to conventional anti-anxiety drugs [82]. Its n-butanol extract showed a beneficial effect in relieving asthma in mice by reducing the eosinophils (EOS) and MDA levels and increasing IL-2, IL-10, IL-12 and SOD levels [83]. Studies report that Chamomile accelerates the healing of skin wounds by promoting fibroblast proliferation and migration [84]. Wan et al. indicated that apigenin in this plant inhibits transforming growth factor β1 (TGF-β1)-stimulated cardiac fibroblasts (CFs) differentiation and extracellular matrix (ECM) production by reducing microRNA-155-5p (miR-155-5p) expression, increasing c-Ski expression, and lowering Smad2/3 and p-Smad2/3 expression [85]. Studies report that chamomile extract abrogates withdrawal behavioural manifestations in morphine-dependent rats [86].

A summary of various pharmacological activities of Chamomile are shown in **Figure 2**.

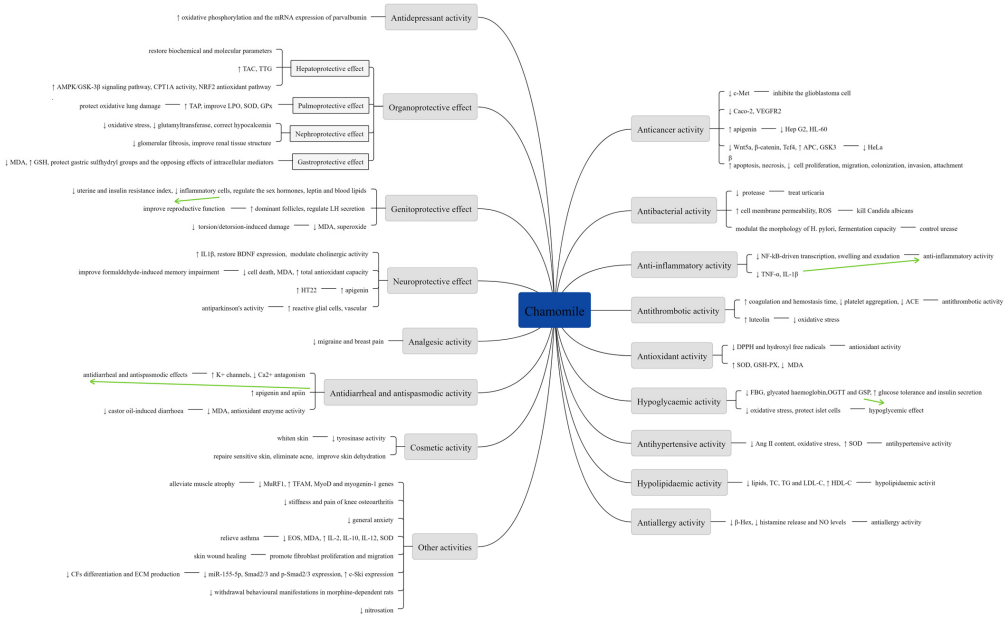

Figure 2. Summary of various pharmacological activities of Chamomile.

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