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Proceeding Paper

Santolina chamaecyparissus L.: A Brief Overview of Its Medicinal Properties †

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Abstract: *Santolina chamaecyparissus*, commonly known as cotton lavender, is a plant with recognized medicinal properties that has been traditionally used for several conditions, including providing relief in premenstrual syndrome and the treatment of infections and digestive disorders. Its extracts have been found to have a range of therapeutic effects and can be used in modern medicine due to their analgesic, anticancer, anti-inflammatory, antimicrobial, antioxidant and antispasmodic properties, or as central nervous system depressants. This work provides the readers with a review of the current research on *Santolina chamaecyparissus*, emphasizing its potential as a novel therapeutic approach in modern medicine, making it a functional food and nutraceutical.

Keywords: *Santolina chamaecyparissus*; medicinal properties; natural compounds

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1. Introduction

Plants have long been used for therapeutic purposes, and therefore many drugs used in modern medicine are derived from natural compounds [1], namely aspirin (from the bark of willow trees, genus *Salix*), digoxin (from the flower of foxgloves, *Digitalis lanata*), morphine (from opium, a dark-brown resin in poppies, *Papaver somniferum*) and paclitaxel (from the Pacific yew, *Taxus brevifolia*) [2,3]. Investigating plant compounds may lead to new, sustainable and cost-effective therapies for various diseases, including diabetes, cancer, osteoporosis and cardiovascular and neurodegenerative diseases [4,5].

Santolina chamaecyparissus L., commonly known as cotton lavender, is a small, evergreen plant native to the Mediterranean region and parts of Europe and America [6]. It is considered an aromatic plant and has been used in Mediterranean folk medicine for a diverse range of purposes. Despite its potential, there is a lack of studies exploring the medicinal properties of this plant. To address this gap, the present work aims to provide the readers with a review of the medicinal properties of *S. chamaecyparissus*, highlighting its importance as a potential source of compounds with therapeutic properties.

2. Medicinal Properties of *Santolina chamaecyparissus*

Even though there have not been many studies addressing the therapeutic benefits of *S. chamaecyparissus*, researchers have demonstrated its potential. Analgesic, anti-inflammatory, antimicrobial, antioxidant, antispasmodic, hepatoprotective, anticancer and antidiabetic properties have been found in this plant's extracts, giving insights into its uses in folk medicine.

2.1. Analgesic

Pain management is a major challenge in modern medicine, and there is a need for novel approaches to treat both acute and chronic pain. Giner et al. (1988) studied the analgesic properties of *S. chamaecyparissus* by testing various extracts (hexanic, chloroformic, ethyl acetate, methanolic) and a lyophilized infusion made from the aerial parts of the plant in thermic and mechanical analgesia tests on mice and rats [7]. Thermic analgesia was determined by administering two doses (300 and 600 mg/kg) of the extracts intraperitoneally (i.p.) and putting male mice on a hot plate. The time that elapsed before each mouse tried to jump off was measured. Mechanical analgesia was performed by i.p. injections of the extracts (300 mg/kg) to female rats one hour before subcutaneous administration of 0.1 mL of λ-carrageenan into the hind paw. Results show that the extracts had activity in both tests, with the hexanic and chloroformic extracts demonstrating the most promising effects, producing a significant increase in response time to both stimuli.

2.2. Anti-Inflammatory

Inflammation is a contributing factor to many acute and chronic diseases [8], including Alzheimer's disease, atherosclerosis, autoimmune, cancer, cardiovascular illnesses, diabetes and rheumatoid arthritis [9]. Giner et al. (1988) evaluated the anti-inflammatory activity of several extracts (hexanic, chloroformic, ethyl acetate, methanolic) and a lyophilized infusion obtained from the aerial parts of *S. chamaecyparissus* using the λ-carrageenan-induced rat hind paw oedema method [7]. Most extracts were only minimally effective at the highest dose, while the chloroformic extract was more effective than phenylbutazone, a nonsteroidal anti-inflammatory drug, at the highest concentration (600 mg/kg) and similar at a lower concentration (300 mg/kg). The lyophilized infusion was also similar to phenylbutazone at 300 mg/kg. Giner et al. (1989) used smooth muscle preparations from rats and guinea pigs to study contractile responses and found that the extracts reduced contractions in guinea pig ilea and rat uteri [10], suggesting that they may antagonize histamine and serotonin, which are known mediators of inflammation [11]. Ríos et al. [12] isolated an active principle (β-sitosteryl 3-β-D-glucoside) from a chloroform extract of *S. chamaecyparissus* and injected it i.p. (50, 75 and 100 mg/kg) and orally (75, 125, and 150 mg/kg) one hour before injecting 0.05 mL of λ-carrageenan subcutaneously into the right hind paw of mice. These authors found that it had a potent anti-inflammatory effect in comparison with phenylbutazone [12]. Cuéllar et al. (1998) used a flower extract of *S. chamaecyparissus* to evaluate its anti-inflammatory properties using topical applications of both 12-*O*-Tetradecanoylphorbol-13-acetate (TPA) and arachidonic acid (AA) to induce ear oedema in female Swiss mice and the phospholipase assay system [13]. The extract inhibited TPA- and AA-induced ear oedema by 67% and 31%, respectively. A methanolic extract obtained from the aerial parts of *S. chamaecyparissus* was used by Sala et al. [14] to study its ability to reduce PLA_2-induced mouse hind paw oedema. They found that it reduced oedema and inhibited the activity of PLA_2 in vitro by 39%. Boudoukha et al. (2016) observed that both an aqueous extract and a polyphenolic extract of *S. chamaecyparissus* reduced the activity of neutrophils, inhibiting their migration and other functions [15]. Djarmouni et al. (2018) found that a crude extract had anti-inflammatory activity using the Phorbol-12-myristate-13-acetate (PMA)-induced male Swiss mice ear oedema model [16]. The extract was administered topically (100 mg/kg) 1 h before PMA topical application, and the pre-treatment with the crude extract reduced ear oedema even more than diclofenac (10 mg/kg), a common clinical nonsteroidal anti-inflammatory drug. Meriem et al. [17]

used a PMA-induced mice ear oedema test to evaluate the anti-inflammatory of several *S. chamaecyparissus* extracts (methanolic, chloroformic, ethyl acetate and aqueous extract). Pre-administration of the methanolic extract (100 mg/kg) markedly inhibited PMA-induced ear oedema, which they attributed to its rich polyphenol content.

2.3. Antimicrobial

Antibiotic resistance and the emergence of new strains of disease-causing agents are major global health concerns driving the need for the development of new pharmaceuticals or alternative drug sources [18]. Suresh et al. (1997) used the two-fold serial dilution technique to determine that a volatile oil extracted from the aerial parts of *S. chamaecyparissus* had potent antifungal activity against *Candida albicans* [19]. Djeddi et al. (2012) found that an *S. chamaecyparissus* essential oil strongly inhibited the growth of *Klebsiella pneumoniae* and *C. albicans*, and moderately inhibited several other bacterial strains (*Bordetella bronchiseptica*, *Escherichia coli*, *Enterococcus faecalis*, *Micrococcus luteus*, *Pseudomonas aeruginosa*, *Saccharomyces cerevisiae*, *Staphylococcus aureus*, *Staphylococcus epidermidis*) [20]. Using the agar diffusion method, Khubeiz and Mansour (2016) found that an essential oil (10% (*v/v*)) extracted from the leaves of *S. chamaecyparissus* exhibited strong antibacterial activity against *Bacillus subtilis*, *K. pneumonia* and *P. aeruginosa*, and inhibited the growth of *C. albicans* and the fungus *Fusarium solani* [21]. Using the same method, Chirane et al. (2019) found that an essential oil extracted from the aerial parts of the plant was able to inhibit the growth of *S. aureus* and *B. subtilis* [22]. The antibacterial properties of both the essential oil and the nano-emulsified essential oil developed by AlMotwaa and Al-Otaibi (2022) were assessed in five different bacterial strains [23]. The most sensitive bacteria strains were the Gram-positive bacteria *S. aureus* and the methicillin-resistant strain *MRSA*.

2.4. Antioxidant

Reactive oxygen species, such as free radicals, can harm both humans and animals. Thus, researchers are searching for effective compounds to protect against their effects [24]. The antioxidant activity of *S. chamaecyparissus* extracts has been evaluated by several authors. Djarmouni et al. (2018) obtained several extracts from the aerial parts of *S. chamaecyparissus* (crude extract, chloroform extract, ethyl acetate extract and aqueous extract). The ethyl acetate extract had the highest phenolic and flavonoid content [16]. This extract and the chloroform extract showed the highest inhibition of xanthine oxidase. Plants high in phenolic compounds that inhibit the xanthine oxidase enzyme without side effects are gaining attention as potential novel drug sources. Allopurinol, their counterpart, is a potent but side-effect-ridden xanthine oxidase inhibitor [25]. Messaoudi et al. (2018) obtained two extracts from the aerial parts of *S. chamaecyparissus*, an aqueous extract and an ethanol extract [26]. Adult male Wistar rats were divided into three groups administered with increasing concentrations of both extracts (30, 150 and 300 mg/kg). Animals were supplemented with the extracts for seven days before carbon tetrachloride (CCl_4) was administered i.p. to induce liver damage. These authors found that hepatic superoxide dismutase and catalase activities were decreased after CCl_4 administration, and treatment with both extracts restored the activity of these enzymes to normal levels.

2.5. Antispasmodic

Antispasmodic drugs are often utilized to manage musculoskeletal tension and anxiety, which usually result in poor quality of life [27]. Giner et al. (1988) explored the effect of several extracts on isolated organs (rat duodenum and uterus) and found that polar extracts (hexanic and chloroformic) exhibited anticholinergic effects, especially the hexanic extract (90 µg/mL), inhibiting acetylcholine-induced contractions of rat duodena and oxytocin-induced contractions of rat uteri [7]. Giner et al. [10] used smooth muscle preparations from rats (duodenum, uterus and vas deferens) and guinea pigs (ileum) to evaluate the contractile responses. The extracts antagonized the contractions of the rat duodenum (acetylcholine-induced), guinea pig ileum (histamine-induced), rat vas deferens (noradrenaline-induced)

and rat uterus (serotonin-induced). Rat duodenum contractions were completely blocked by the hexanic extract at 900 μg/mL, while guinea pig ileum contractions were antagonized by all extracts in a concentration-dependent manner.

2.6. Hepatoprotective

The liver is a vital organ that plays numerous important roles, including the metabolism of proteins, lipids and carbohydrates [28]. Acute and chronic liver diseases are a significant global health problem, and current medical treatments may be inadequate or challenging to carry out [29]. Messaoudi et al. (2018) evaluated the hepatoprotective effects of *S. chamaecyparissus* in CCl_4-intoxicated male Wistar rats by supplementing them with three different concentrations of two extracts (aqueous and ethanol extracts) of the aerial parts of this plant [26]. These researchers found that supplementation with both *S. chamaecyparissus* extracts reduced the concentration of serum markers, which increases with liver damage [30]. The extracts also protected against steatosis and hepatocytic necrosis by stabilizing cell membranes and repairing liver damage caused by CCl_4 exposure.

2.7. Anticancer

Finding effective and safe cancer treatments is a major goal in modern medicine, as many traditional treatments are toxic to both cancer and normal cells [31]. Several studies have investigated the anticancer effects of *S. chamaecyparissus* extracts and essential oils. Elsharkawy (2014) demonstrated that an essential oil obtained from the aerial parts of *S. chamaecyparissus* had high cytotoxicity against a human hepatocellular carcinoma cell line (HepG2) at doses of 100 and 50 μg/mL using a 3-(4,5-dimethylthiazol-2-yl)-2,5-diphenyltetrazolium bromide (MTT) assay [32]. A hydromethanolic extract of the aerial parts of the plant rich in triterpene compounds was shown to have high cytotoxicity in the MTT assay against HepG2 at a dose of 100 mg/mL and in a human lung adenocarcinoma cell line (A549) at doses of 50 and 100 mg/mL [33]. Saygideger et al. (2021) found, via the scratch assay, that an essential oil from the leaves of *S. chamaecyparissus* had high cytotoxicity in the MTT assay and caused loss of cell motility in the non-small-cell lung cancer cell lines A549 and SA7 at concentrations of 92–100 μg/mL and 200–240 μg/mL, respectively [34]. Ali et al. (2021) used an ethyl acetate leaf extract of *S. chamaecyparissus* at a concentration of 100 μg/mL in a human breast cancer cell line (MCF-7) and found that it led to a negative expression of the epidermal growth factor receptor, which is involved in cancer development when overexpressed [35]. Additionally, a nano-emulsion containing essential oil from *S. chamaecyparissus* was obtained to improve the use of essential oils [23], due to their volatility and poor aqueous solubilities. The pure essential oil was more effective in reducing the viability of cancer cells than the reference drug (gemcitabine) and nano-emulsion, but the latter was still comparable to gemcitabine. *S. chamaecyparissus* shows potential as a natural anticancer drug source based on in vitro studies, but further research, including in vivo studies, is needed to fully understand its mechanisms and potential clinical use for cancer treatment.

2.8. Antidiabetic

Diabetes, particularly *type 2*, is a rapidly increasing global issue with numerous complications, such as cardiovascular disease, ischemic heart disease, peripheral vascular disease, retinopathy, neuropathy, and nephropathy [36]. Ali et al. (2021) investigated the antidiabetic properties of *S. chamaecyparissus* using an ethyl acetate leaf extract in an in vitro α-glucosidase assay [35]. The extract was able to reduce this enzyme's activity, which is responsible for breaking down disaccharides into absorbable monosaccharides, namely glucose, which are absorbed, resulting in hyperglycemia.

2.9. Other Medicinal Properties

Giner et al. (1988) explored the antiulcerous activity of several extracts (hexanic, chloroformic, ethyl acetate, methanolic) obtained using a stress-induced female Sprague

Dawley rat ulcer model, and all exhibited antiulcer activity at the concentrations tested (125, 250 and 500 mg/kg), except the hexanic extract, which only demonstrated anti-ulcer activity at the highest concentration [7]. These authors also evaluated spontaneous activity of female mice using an Animex S counter after i.p. injection with the extracts [7]. All extracts led to a reduction in spontaneous activity, especially the chloroformic extract.

3. Concluding Remarks

Medicinal plants, such as *S. chamaecyparissus*, have been used for a long time in folk medicine and are known to have a range of beneficial properties. These properties are often attributed to the presence of phenolic compounds, which are known to have antioxidant effects, among others. *S. chamaecyparissus* has been shown to have analgesic, anticancer, antidiabetic, anti-inflammatory, antimicrobial, antioxidant, antispasmodic, antiulcer and hepatoprotective effects in both in vitro and in vivo studies. Further research is warranted to fully understand the mechanisms behind these effects and to determine the potential clinical applications of *S. chamaecyparissus* for human disease treatment.

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