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Mustehasan
Central Council for Research in Unani Medicine, Ministry of AYUSH, Government of India, New Delhi-110058, India

Kadija A. Hafiz
Drug standardization Research Institute, PCIMH Building, Kamla Nehru Nagar Ghaziabad-201002, Uttar Pradesh, India

Mohammad Jameel
Drug standardization Research Institute, PCIMH Building, Kamla Nehru Nagar Ghaziabad-201002, Uttar Pradesh, India

Asma S. Khan
Drug standardization Research Institute, PCIMH Building, Kamla Nehru Nagar Ghaziabad-201002, Uttar Pradesh, India

Kamran Ashraf
Faculty of Pharmacy, Universiti Teknologi MARA (UiTM), Cawangan Selangor, Kampus Puncak Alam, Bandar, Puncak Alam, Selangor Darul Ehsan, Malaysia

Correspondence:
Dr. Mohammad Jameel
Drug standardization Research Institute, PCIMH Building, Kamla Nehru Nagar Ghaziabad-201002, Uttar Pradesh, India
Email: ahmadjamil84@gmail.com

Traditional and pharmaco-therapeutical landscape of Brinjasif (*Achillea millefolium* L.): An important medicinal plant in the traditional AYUSH system of medicine

Mustehasan, Kadija A. Hafiz, Mohammad Jameel, Asma S. Khan, Kamran Ashraf

ABSTRACT

Achillea millefolium, multipinnate, pubescent herbaceous flowering plant, distributed from Europe to Asia, is illustrated globally as Yarrow in English and Brinjasif in Greco-Arab tradition. The genus '*Achillea'* is believed to wound healing traditional resource since ancient times. It is also used in various ailments like spasmodic pain of gastrointestinal tract, hepato-biliary and gynecological issues, cholagogue along with neuroprotection in traditional medicinal systems. Reported pharmacological activities of Brinjasif are antiulcer, analgesic, antimicrobial, anti-diabetic, antifungal, anti-inflammatory, antioxidant, antiseptic, antitumor, hemostatic, hepato-protective action due to presence unique natured and diverse class of phyto-molecules including sesquiterpenes, monoterpenes, flavonoids, phenolic compounds, lactones, and coumarins. This review has highlighted the significant applications of this medicinal plant in traditional systems. Furthermore, it will provide evidence-based information for understanding molecular mechanisms in future research.

Keywords: *A. millefolium*, Brinjāsif, Mizaj, Unani medicine, AYUSH system.

INTRODUCTION

A. millefolium is a perennial herb, widely distributed in the world, from Europe to Asia, growing in temperate to arid environments [1]. It has 130 species in temperate Asia and North America, and Europe. There are 46 genera in Turkey and Iran [2]. In India, it is generally found in the Himalayas from Kashmir to Kumaon at altitudes ranging from 1050 to 3,600 m [3-5]. In Greek tradition, Achillea is used as a wound healing product [6], also described in the Elder and Dioscorides, which are among the oldest surviving texts in the classical European medical tradition [7].

Unani Description It is widely found on the banks of rivers and streams, and has a sticky, viscous liquid appearance at the touch, of two varieties; one has small branches but larger leaves with yellow flowers, with the characteristic smell of absinthe, and the other has smaller, thinner leaves with white flowers, and is known as Qayṣūm. Galen stated that both species (Brinjāsif and Qayṣūm) have the same temperament and are collectively referred to as Brinjāsif [8-11]. Interestingly, Pliny's Natural History identified the plant as yarrow and taxonomically identified it as achillea, which is considered to be a valuable healing plant [12]. In addition, Achillea is referred to in the classical Unani literature as Arṭāmāsīa, Artiyamasia and Brinjāsif [8-9]. It has been used in the Greco-Arabic system for centuries as an herbal food, various gastrointestinal disorders, headaches, hepatobiliary disorders and dermatological conditions [13-15]. Decoctions, fresh juices and infusions have been used for the treatment of anorexia, enteritis, flatulence, gastritis, abdominal pain, cough, diarrhea, menstrual bleeding, wounds, sores and skin rashes, as well as dog and snake bites [16-17].

Vegetal description

A. millefolium is a perennial herbaceous plant (Figure 1). Its height varies up to 50 cm. A slender stem with numerous roots and stolon, with a blunt, juicy scale at each node. The leaves are almost feathery, bipinnate or tripinnate, hairy (pubescent) and arranged spirally at the mid-stem and at the end of the leaf. The head flower is composed of 5-6 ray florets and 12–24-disc florets, white or purplish, ovoid and with a flattened base The petals are arranged in flattened piles. The fruit is 2 mm in length, shiny, oblong achenes with broad wing edges without pappus [18-19].

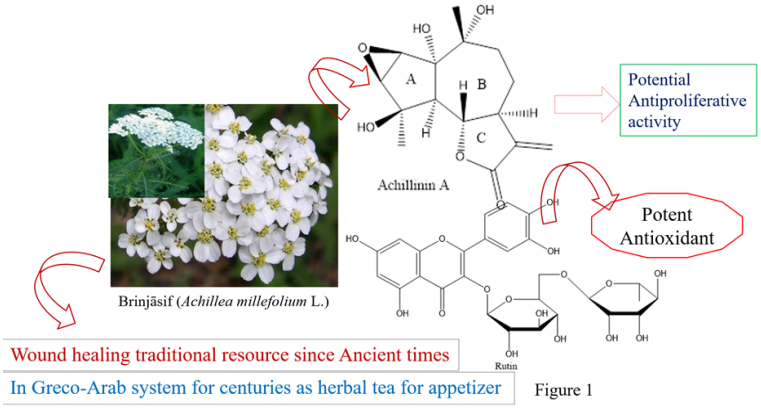


Figure 1: Brinjasif flower with aerial parts

Vernacular names

It is described with numerous synonyms in different traditional cultures as mentioned below.

Unani:	Brinjāsif, Arṭāmāsyā [8-9]
Arabic:	Shawylā, Qayṣūm [8-10]
Persian	Bumādarān [10]
English:	Bloodwort, Milfoil, Stanchgrass, Thousand-leaf, Yarrow [3,5,20].
Hindi:	Bhutkesi, Gandmār, Puthkanda [8,21].

Persian literature

In the folk Iranian script, it is referred to as Bumadarān and is used for various ailments such as pain, inflammation and gastrointestinal disorders. Its dried flowers are useful in reducing the size of the stools, dyspepsia, dysmenorrhea and gastritis [22], menstrual problems, as a diuretic, tooth pain and sedation [23], burns and injuries [24].

Pharmacological properties

Medicinal plants are major source of novel and complex structured phyto-molecules due to their wildly survival nature and resulting to development of vibrant class of chemotypes and that are utilized as multiple reasons since ancient times [25]. Their parts are playing significant role in remedial therapy [26] due to the presence of several chemical components, including essential oils, sesquiterpenes and phenolic compounds. They are associated with a number of pharmacological effects, such as analgesic, anti-diabetic, antifungal, anti-inflammatory, antioxidant, antiseptic, antitumour, cholagogue, haemostatic, hepatic protection and spasmolytic [1,13,15,27-31]. In addition, its tea is used to treat digestive problems, flower decoctions or tinctures, infusions or capsules reduce the pain of primary dysmenorrhea [32-34]. The purpose of their practices is often passed verbally from one generation to the next [35]. It is significant to explore such plants to progress understanding of their properties, security, and usefulness [36], as well as prevention of destructive changes in the knowledge during transmission from one generation to the next [37].

Chemical constituents

Several phyto-compounds including caffeic acid derivatives, sesquiterpenes, monoterpenes, flavonoids, and phenolic compounds have been reported from Brinjāsif. Its most of the important constituents are summarized in below.

Temperament (*Mijaz*): Hot 1° & Dry 2° [8,10,38]; Cold & moist [11].

Unani Pharmacological actions (Af'al)

Mulattif (demulcent), *Mufattiḥ-i-Sudad* (deobstruent), *Qāṭi'-i-balgham* (remover of phlegm), *Qātil-i-Dīdān-i-Am'ā'* (anthelmintic), *Muḥallil –i-Waram* (antiinflammatory), *Dāfi'-i-Ḥummā* (antipyretic), *Muṣaffī-i-Dam* (blood purifier), *Mujaffif* (drying agent), *Mudirr-i-Bawl* (diuretic), *Mudirr-i-Ḥayḍ* (emmenagogue), *Mufattit-i-Ḥaṣāt-i-Gurdah wa Mathāna* (lithotryptic) [8-11,20,38].

Traditional therapeutic applications

1. Neurological ailments: Its *Ḍimād* (local application), *Naṭūl* (irrigation) and decoction relieves various type of headache. Inhalation of its decoction's vapours are useful in nasal passage, coryza, *Sarsām Balghamī* (phlegmatic meningitis), *Subāt* (coma) and relieves obstruction of brain vessels causing paralysis. It is also useful as brain tonic. Irrigation of its decoction also useful in *Sadr-o-Duwār* (dizziness and vertigo) [8-11,38].

2. Respiratory ailments: Its inhalation and *Ḍimād* also relieves chest pain. The smell of its flower also cures the common cold. Decoction of its fruit relieves the constriction of the bronchial passages. Taking decoction of the fruit with quince fruit reduces the swelling of the throat [8-11,38].

3. Urogenital ailments: Plant ash with wine is used to dissolve kidney stones. Its decoction controls menstrual irregularities, while local application to the lower abdomen speeds up the onset of menstruation and urination. Oral administration and topical application are beneficial for ulcers, releasing the fetus and the placenta, opening the womb mouth and removing the hardiness. Its extract, taken with myrrh when used as vaginal pessary, clears away the dirt. Drying her ashes in the vaginal area will dry out excessive moisture [8-11,38].

4. Gastrointestinal ailments: Plant ash in 10.5 g quantity is used with honey to expel intestinal worms [8-11].

5. Miscellaneous use: Decoction of Brinjāsif is useful in fever. Its leaves are used to repel insects and pests. Its leaves with wine are valuable in scorpion bites. Dusting off plant ash heals the wounds [8-11,38].

PRECLINICAL STUDIES

Antiulcer

The antiulcer activity of Brinjasif is assessed with aqueous extract against gastric ulcers induced by ethanol in rats. The results unveiled that the antiulcer activity of extract was due to inhibition of gastric secretion or increase in blood flow (protective factor) in gastric mucosa [39]. Potrich *et al*., has evaluated the efficacy of hydro-alcoholic extract of the aerial part of Brinjasif orally and found that it reduced gastric lesions significantly [40]. Similarly, Borrelli *et al*., examined gastric motility [41]. The results revealed that water extract

contracted human and mouse gastric strips and also found contraction effect was unaffected by hexamethonium and tetrodotoxin, however it is reduced by atropine. Sedighi *et al*., suggested locomotors activity of ileum in Wistar rats with aqueous extract of Brinjasif [42].

Hepatoprotective

Gadgoli and Mishra *et al*. assessed antihepatotoxic activity of floral extract of Brinjasif on Wistar rats and estimated the serum transaminase *viz*., total bilirubin, Glutamyl Oxaloacetate Transaminases (SGOT, Glutamyl Pyruvate Transaminase (SGPT), Glutamic pyruvate Transaminase [43].

Antidiabetic potential

Zolghadri *et al.* has investigated the effect of Brinjasif as a traditional hypoglycemic agent in adult male Wistar rats [44]. The effect was reported on IL-1β and iNOS gene expression of pancreatic tissue in the streptozotocin (STZ) induced diabetic rats. The results revealed that the extract caused significant reduction in both IL-1β and iNOS genes expression. The extract caused beneficial effects on STZ-induced diabetic rate due to amelioration of IL-1β and I NOS gene over expression which can have a β-cell protective effect.

Anticancer

Amir-ghofran and Karimi *et al*. investigated anticancer properties of ethanolic extract of aerial parts of yarrow plant were reported on leukemia cell lines and human breast cancer [45]. The plant extract resulted in 50% inhibition of SK-Br and K 562 cells. Csupor-Löffler *et al.* extracted Casticin from *A. millefolium* and their antitumor properties were evaluated through cell cycle and apoptotic signaling pathways in two MCF subline MN1 and MDD2 [46]. The result revealed that the lines were found sensitive to Casticin and stopped the cell growth at G2/M phase and induced apoptotic death by acting as a tubulin binding agent (TBA). Similarly, anticancer potential of ethanolic extract of Brinjasif was evaluated on normal fibroblast cell line (HFFF), and many more cancerous cell lines [47]. Hemmati *et al.* anticancerous properties of Brinjasif flower extract was investigated on bleomycin- induced lung fibrosis in Sprague Dawley rat [48]. No toxicological or histopathological abnormalities were recorded in rats after the treatment, moreover, less contraction of lung strips was observed after the treatment.

Anti-Inflammatory

Benedek *et al.* assayed the aqueous and methanolic extract of *A. millefolium* for anti-inflammatory activity [14]. They found that the extract and the flavonoid-enriched fraction inhibit inflammation significantly due to presence of glycosylated phenolic compounds *viz*., apigenin-7-*O*-glucoside, luteolin-7- *O*-glucoside and caffeic acid. Burk *et al.* examined the effects of aqueous extract of Brinjasif on the inflammatory responses on cell lines [33]. The study clearly suggested the potential of *A. millefolium* to combat acute and chronic inflammation.

Antioxidant

Vitalini *et al.* explored ethanolic extract of Brinjasif flower might be used as antioxidant by DPPH, total antioxidant capacity (TAC), copper reducing power and TBARS assays [49]. The extracts showed the promising antioxidative responses with respective models. Compound like rutin, luteolin-7-*O*-glucoside and chlorogenic acid showed the highest activity while luteolin-7-*O*-glucoside and apigenin-7-*O*-glucoside showed the maximum inhibition of TBARS formation. Kazemi *et al*. evaluated the antioxidant activity of several compounds isolated from essential oil of the aerial parts of Brinjasif and analyzed using DPPH assay [50]. The highest scavenging capacity against DPPH was recorded for Thymol followed by carvacrol, and the lowest activity was exhibited by bornyl acetate. However, similar activity was observed in α-pinene, limonene and camphene. Georgieva *et al.* reported the antioxidant activity of Brinjasif (leaves and stems decoction) [51]. The highest antioxidant activity was observed for CUPRAC followed by FRAP, DPPH and ABTS.

Antimicrobial

Stojanovic *et al.* tested the extracts of aerial parts of Brinjasif for antimicrobial activity in a disk diffusion assay against five bacteria (*E. coli, K. pneumoniae*, *P. aeruginosa*, *S. enteritidis* and *S. aureus*) and two fungi (*Aspergillus niger* and *Candida albicans*) [28]. The plant extract showed the antimicrobial activity against all the tested microbes. Hasson *et al.* determined the antimicrobial activity of ethanolic and aqueous extract of the flower against *Enterococcus faecalis* [52]. *Micrococcus luteus*, *Salmonella enterica*, *pseudomonas aeruginosa*, *Shigella flexneri* and *Staphylococcus aureus* using the diffusion test method. Turker *et al.* found the antibacterial activity of extract of Brinjasif against g-positive bacteria (*S aureus, S. epidermidis and S. pyogenes*) [53]. Maz *et al.* studied antibacterial activity of essential oil derived from Brinjasif plant against 9 g positive and 2 g negative bacteria [54].

Gastroprotective Activity

Cavalcanti *et al*. studied antiulcerogenic activity of crude aqueous extract of *A. millefolium* [13]. The extract protects the gastric mucosa against the necrotic action of ethanol and stress-induced lesions by reducing the volume and acidity of secreted gastric juice. The protective action of extract must be due to the blockage of the mainly receptors presented in the parietal cell as well as their secondary messengers. Similarly, Potrich *et al*. reported that Hydro-alcoholic extract of yarrow reduced the chronic gastric ulcers and promoted significant regeneration of the mucosa [40].

Neuroprotective Effect

Vazirinejad *et al*. reported that the aqueous extract of Brinjasif ameliorates disease severity, inflammatory response and demyelinating lesion in experimental autoimmune encephalomyelitis because of its anti-inflammatory and antioxidant properties [55].

Anti-fertility

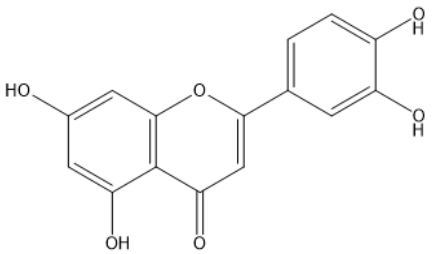
Takzare *et al*. reported anti-fertility activity in adult male Wister rats induced by aqueous extract of *A. millefolium* [56]. The decrease sperm count has seen at the dose of 800 mg/kg of extract by intra peritoneal injection. Thickened seminiferous, tubules on basal membrane and decrease in cell accumulation in seminiferous tubule has also recorded.

Analgesic Activity

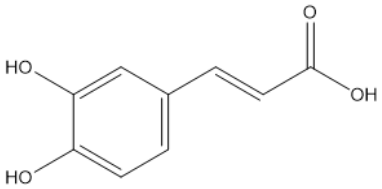
Pires *et al.* has found anti-analgesic effect of extract from *A. millefolium with in vivo* studies due to existence of flavonoid glycoside, rutin and caffeic acid [57]. Similarly, Noureddini *et al.* has exhibited antinociceptive effects of plants [58]. Amiri *et al*. investigated traditional Iranian edible plants in similar activity due to rich in chemo diversity pattern of plant [59].

Wound healing and miscellaneous potential.

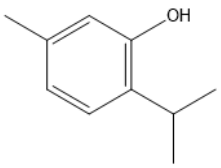
Hemmati *et al.* has reported healing property of 5% yarrow extract *in vitro* study with complete curing after 14 days of treatment [60]. Ghasemi *et al*. suggested wound healing effects of *A. millefolium* essential oils along with antibacterial activity [61]. Similarly, Sayed and Bano *et al.,* reported Brinjasif as anti-inflammatory, analgesic, antipyretic, diuretic, emmenagogue, and anti-helminthic potential [62].



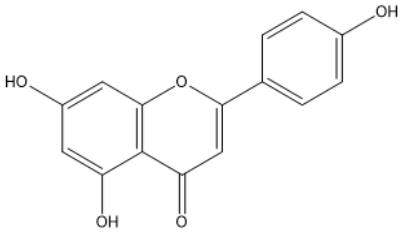
Luteolin



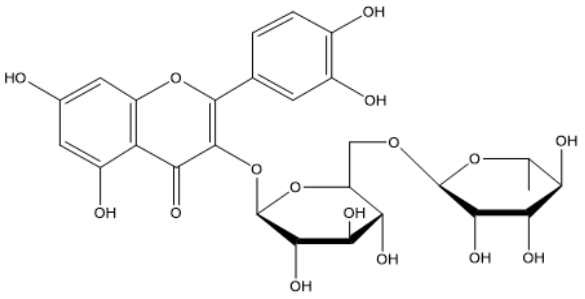
caffeic acid



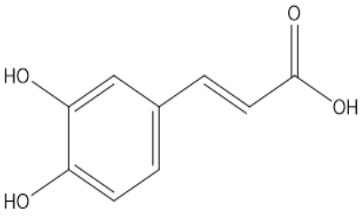
thymol



Apigenin



Rutin



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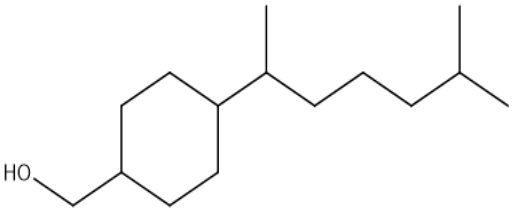
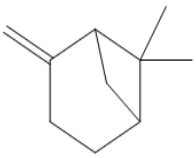
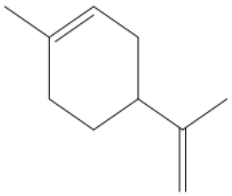
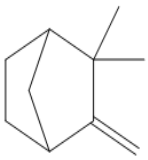
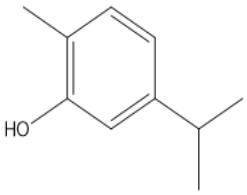


Bisabolol

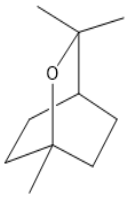

Bita pinene


Limonene


Camphene



Carvacrol



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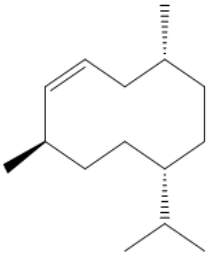
Germacrene

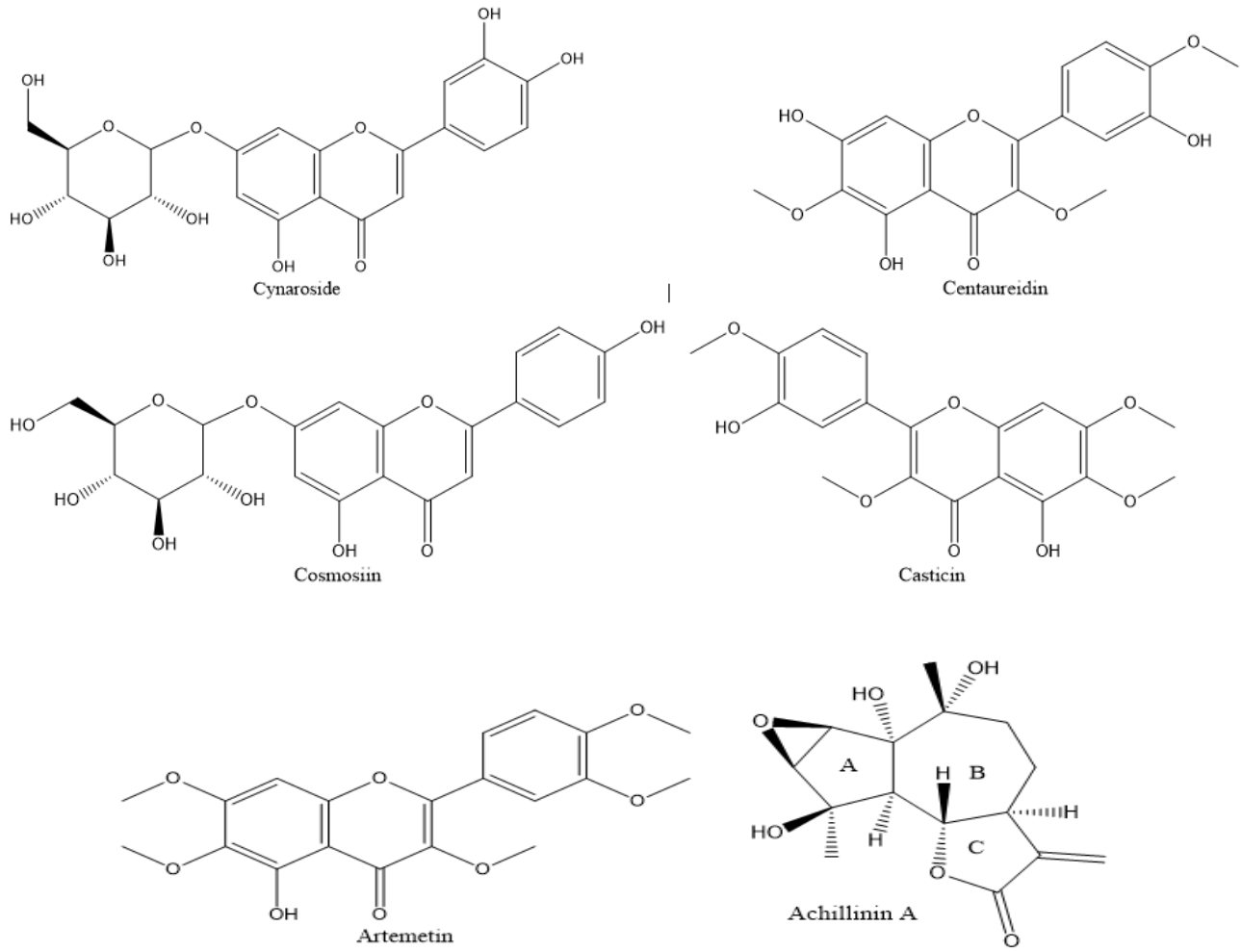

Figure 2: Phytochemicals of *A. millefolium and* their chemical properties

CONCLUSION

It is important to investigate these plants to understand their properties, safety and efficacy, and to avoid harmful changes in knowledge about medicinal plants during the transmission from one generation to the next. Brinjasif has worldwide widespread therapeutic use with outstanding pharmacological activity due to the presence of very unique and crucially un-unmatched secondary metabolites. Its ancient traditional values have been scientifically confirmed by some pharmacological properties, and there are many more revelations that are yet to be made. This article will be fruitful and will be a necessary step in the discovery of further clinical and molecular research which will prove valuable in exploring the therapeutic potential of this plant at a more profound level.

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Conflict of interest

The authors declared no conflict of interest.

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