Yarrow (*Sultaani Buti/ Barinjasif*): Famous Aromatic and Medicinal Herb of Pakistan

Muhammad Akram[1,*], Syed Ahmed Shah[2] and Mahwish Ahmed Karim[3]

[1]*Department of Pharmacology, Faculty of Pharmacy, University of Sindh, Jamshoro*

[2]*Department of Pharmacognosy, Faculty of Pharmacy, University of Sindh, Jamshoro*

[3]*Department of Pharmacognosy, Faculty of Pharmacy and Pharmaceutical sciences, University of Karachi*

Abstract: *Barinjasif* is well grown in Pakistan. It is included in several pharmacopoeias and is used commercially in the preparation of a variety of pharmaceutical preparations including teas, tinctures, liquid extracts and also in compound herbal preparations. *Achillea millefolium* L. is used as astringent, lithotripsic agent and antimicrobial and is an antiseptic to urinary infections. It is diaphoretic, antihypertensive, cholagogue, spasmolytic, antispasmodic and it is used topically for wounds and as anti edema and anti-inflammatory while orally for fever, common cold, digestive and carminative. Its use has been documented in varicose ulcer, cuts and injuries. It is also found very effective in leucorrhoea and all kinds of piles. It is a cleansing agent for which they are of high demand in the cosmetic industry to be used in skin and hair preparations. It promotes healing and cleansing.

Keywords: *Barinjasif*, Pharmacopoeia, Pakistani plant, Cosmetic industry, Cleansing agent, Healing.

INTRODUCTION

Plant belongs to family *Asteraceae Bercht. & J. Presl* {O Prirozenosti Rostlin 254. 1820. (Jan-Mar 1820) (Prir. Rostlin)}, the largest family of Angiosperms, comprises of ± 1535 genera and c. 23000 species distributed in 3 subfamilies and 17 tribes. The number of genera is rather increasing as more than 10 genera are described each year and several are resurrected from or reduced to synonyms. (Bremer, K. 1994. Asteraceae-Cladistics & Classification, Timber Press, Portland, Oregon). It is also the largest plant family in Pakistan, represented by over 650 species distributed in 15 tribes.

A. millefolium is native to Asia, Europe and North America, now widely distributed and cultivated in the temperate regions of the world. *Achillea borealis* Bong., *A. lanulosa* Nutt., *A. magna* auct., *A. millefolium* ssp. *borealis* (Bong.) Breitung., *A. millefolium* ssp. lanulosa (Nutt.) Piper, *A. millefolium* var. *occidentale* DC are the synonyms of the plant. In English, known as carpenter's weed, milfoil, hierba de las cortaduras, bloodwort, plumajillo, common yarrow, western yarrow, yarrow (common). In urdu/unani name is Sultani booti and barinjasif [1-6].

The whole herb is used medicinally (essential oil, plant, flowers, dried flowers, seeds, leaves and powdered drug). The plant is attractive, aromatic, erect, leafy, perennial herb growing upto 30 cm high. Flowers are white heads, corymbose ovoid, shortly pedunculate. Leaves are oblong lanceolate, 2-3 pinnatisect, minutely divided into linear dentate, mucronate segments (Figures **1** and **2**) [7, 5].

Scientifically, the fractions of methanolic extract of the herbal parts of the plant were tested against *Candida species* and *Bacillus cereus* and a fraction showed activity against *Candida spp*. [11]. A little later, it was reported that the antimicrobial activity of the hexane:ether:methanol extract (1:1:1) of *Achillea millefolium* L. aerial parts against some clinical pathogens [12]. In the same year, another study showed the same of ethanolic tincture of stems or flowers of *Achillea millefolium* [13].

More over, *Achillea millefolium* L. alone, as well as in combination proved to possess antimicrobial activity against oral pathogens [8]. Later, a study on chemical constituents of *Achillea millefolium* (*e.g*. apigenin) and showed that its topical applications, twice daily (total of six applications), resulted in lower amounts of polysaccharides in the *Streptococcus mutans* biofilms [9].

In addition, essential oil was reported to possess insecticidal activities [37 - 40]. However, some phytoconstituents were found to be responsible for contact dermatitis [28].

PHARMACOLOGICAL ACTIVITIES

Oral Pathogens

Achillea millefolium (yarrow), alone, as well as in combination with *Juniperus communis (juniper)* and *Urtica dioca (nettle)* have been reported to possess

*Address correspondence to this author at the Department of Pharmacology, Faculty of Pharmacy, University of Sindh, Jamshoro, Pakistan;
Tel: +92-3332965493;
E-mail: akramkhatrisu@yahoo.com; akram.khatri@usindh.edu.pk

Figure 1: Diagrammatic representation of *Achillea millefolium.*

antimicrobial activity against oral micro-organisms: *Streptococcus mitis, Actynomyces viscosus, Actynomyces naeslundii, Actinobacillus actinomycetemcomitans, Prevotella intermedia, Campylobacter rectus, Fusobacterium nucleatum* and *Veillonella parvula* [8]. Later, Koo and coworkers in 2003 studied on chemical constituents of *Achillea millefolium* (*e.g*. apigenin) and showed that its topical applications, twice daily (total of six applications), resulted in lower amounts of polysaccharides in the *Streptococcus mutans* biofilms. Among the different polysaccharides affected by the test agents, alkali-soluble glucans are particularly important for biofilm development and accumulation [9]. A little later, it was observed that in the concentration of 500 and 1000 µg/ml, the dichloromethane and methanol extract of the aerial parts of the plant was unable to show any antimicrobial activity against *Bacillus cereus* var *mycoides* (ATCC 11778), *Bacillus pumilus* (ATCC 14884), *Bacillus subtilis* (ATCC 6633), *Bordetella bronchiseptica* (ATCC 4617), *Micrococcus luteus* (ATCC 9341), *Staphylococcus aureus* (ATCC 29737), *Staphylococcus epidermidis* (ATCC 12228), *Escherichia coli* (ATCC 10536), *Klebsiella pneumoniae* (ATCC 10031), *Pseudomonas aeruginosa* (ATCC 9027), *Streptococcus faecalis* (MTCC 8043), *Candida albicans* (MTCC 10231), *Aspergillus niger* (MTCC 1344), and *Saccharomyces cerevisiae* (ATCC 9763) [10].

Antimicrobial Agent

The methanolic extract of the herbal parts of the plant was fractioned to separate the water soluble and water insoluble parts of the extract. The former was inactive against test organisms while the later have some activity against *Candida albicans, Candida crusei* and *Candida prefringes* with the zone of inhibition of 12mm for each. And for *Bacillus cereus* in the same study the value is 10mm. While, this part was inactive against *Staphylococcus aureus* ATCC #25923, *Streptococcus pneumoniae* ATCC #49619, *Moraxella catarrhalis* ATCC #49143, *Bacillus cereus* ATCC #11778, *Acinetobacter lwoffii* ATCC #19002, *Enterobacter aerogenes* ATCC #13043, *Escherichia coli* ATCC #25922, *Klebsiella pneumoniae* ATCC #13883, *Proteus mirabilis* ATCC #7002, *Pseudomonas aeruginosa* ATCC #27853, *Clostridium perfringens* KUKENS-Turkey, *Mycobacterium smegmatis* CMM 2067, *Candida albicans* ATCC #10239 and *Candida krusei* ATCC #6258. Water soluble part was used in the solution form by dissolving it in phosphate buffer saline (pH 7.0–7.2) and the concentration is 10 mg/ml

Figure 2: Upper from left to right: Plant, White flowers; Lower from left to right: Florets, dried achenes (Crude drug), Powdered dried achenes, Upper surface of leaf. Drug; Lower left: Transverse section of Seeds.

while that the water insoluble part is dissolved in dimethyl sulfoxide (DMSO) with the same concentration [11]. It was reported that by disk diffusion method, the hexane:ether:methanol extract (1:1:1) of

Achillea millefolium L. aerial parts, collected in full bloom from River banks of River Nisava, Nis and Serbia, exhibited antimicrobial activity against *Pseudomonas aeuroginosa, Staphylococcus aeureus, Candida albican, Salmonella enteritidis, Aspergillus niger* and *Eschericheae coli* with no activity at all against *Klebsiella pneumonia* [12]. In the same year, another study showed that ethanolic tincture of stems or flowers of *Achillea millefolium* at the average concentration of 26µg/ml showed 2.5 mm zone of inhibition at 12 hours and 18 hours of incubation against *Staph. aureus* while, in the same condition the extract is inactive against *E. coli* and *Pseudomonas aeuroginosa* [13]. Moreover, the essential oil of the plant *Achillea millefolium* was tested against a variety of agricultural plant pathogenic microorganisms and it was observed that the oil at the volume of 12.5 µl gives the zone of inhibition in the range of 7 to 22 mm and for most of the microorganisms tested the concentration was found bactericidal. In the same study, the MIC values of the essential oil were found in the range of 125 to 250 µl/ml [14]. However, it was reported that distillation waste of *Achillea millefolium,* which was produced during extraction of essential oil from the plant, when evaluated for the antimicrobial, antifungal, antimalarial and anti leishmanial activities, but failed to produce any significant result [15].

Antiproliferating Effect

Achillea millefolium constituents were checked for their antiproliferating activity on three human cancer cell lines that included HeLa, MCF-7 and A431. Centauridine from the plant was proved to be the most effective among other compounds of the plant. It had an IC50 value of 0.0819–0.3540 µM [16].

Antioxidant Activity

Another compound prepration containing *Achillea millefolium* was tested *in vitro* for its antioxidant and thus hepatoprotective activity. The mechanism of action of preparation was suggested that it helped in increasing the levels of antioxidant enzymes superoxide dismutases. The preparation was proved to be antioxidant [17].

Effect on Wound Healing

Effect of *Achillea millefolium* was tested for wound healing in rabbits. The effect of extract was tested against 10 % povidone iodine and 0.9% sodium chloride solution. Daily topical application of the extract showed significant activity in accelerating wound healing [18].

Reduction of Ulcer Size

It was found that the hydro alcoholic plant extract was significantly effective in reducing the size of ulcer as compared to systemic glucantine in treating cutaneous leishmaniasis when tested in mice. The use of the extract in clinical trials was thus suggested [19].

Analgesic Activity

Analgesic activity of the plant extract was proved by rat's formalin test. Aqueous extract of the plant in the doses of 80, 120 and 360 mg/kg orally administered to rats were found to have significant analgesic activity when tested by rat's formalin test [20].

Antiinflammatory Activity of the Plant

Fractions and individual compounds from the *Achillea spp*., has been tested for their anti-inflammatory activity by the method of respiratory burst assay. The results were compared with Indomethacin, a clinically proven NSAID, and concluded that the extract of the whole plant, its fractions and some main constituents from the flowers' head have comparable or more anti-inflammatory activity to the reference drug [21].

Antidiabetic Activity

Antidiabetic activity of the plant decoction was proved and it was found that it decreases the level of epinephrine and blood glucose in the experimental animals while it does not increase the level of insulin. The activity was checked on two models: a. alloxan induced diabetic model, and b. epinephrine induced hyperglycemia [23].

In the Treatment of Ulcers

Achillea millefolium extracts were found to protect the animal models *i.e*. rats from the ulcerative effects of indomethacin, acetic acid and ethanol. It was proposed that the gastric protective effect of the extracts and fractions were due to their activity of increasing the level of an anti-oxidant glutathione and thus behaves as the cytoprotective agent [24].

To Assess the Risk of Mutagenicity

The risk of mutagenecity of the aqueous extract of the fresh plants was assessed *in vitro* by measuring

their chromosomal alteration and breaking activity in human lymphocytes, keeping mitomycin C and Ara-C as the reference drugs. It was found out that the plants themselves were not mutagenic but they had an influence on the clastogenic activity of these mutagenic drugs. *Achillea millefolium* alone in the concentration of 3.5 µg x 10^{-4} g/ml and the same concentration in combination with Ara-C ($5x10^{-7}$ µg /ml) and mitomycin C (0.30 µg /ml) respectively were tested for chromosome breaking activity. It was seen that the plant extract alone was unable to give significant clastogenic activity but with the combination of an alkylating agent, mitomycin C, it gave an additive effect to the activity of mitomycin C and increased both the count of chromatid and isochromatid breaks as compared to the use of mitomycin alone [25].

Contact Allergy from Yarrow

Yarrow is one of the causes of allergic contact dermatitis [26]. Cytokine from t-lymphocytes were high in patients contacted with composite family plants including yarrow as seen by patch test [27].

Two peroxides were extracted from ether fraction of yarrow flowers; α-peroxyachifolid (I) and β–peroxyisoachifolid (II) (Figure: **3**). α–peroxyachifolid (I) was found to be related to contact dermatitis from the plant [28]. Another study from some of the same investigators, in the same year and with the same aim of investigating the principal responsible for contact dermatitis in the blossoms of plants reported that Peroxyachifolid I and II were the compounds that were having the intense sensitizing property when tested on guinnie pigs. While according to their investigations, other constituents of the plant (pontica epoxide and dehydromatricaria ester) were not responsible [29].

Mechanism of Action of Analgesic Activity

An animal study testing the analgesic effect of the plant suggested non-norcotic analgesic effect of the hydroalcohol extract of the plant. Testing the plant hydroalcohol extracts (500 and 1000 mg/kg) with different analgesic mechanisms, in order to figure out its possible mechanism of action in analgesia, concluded that the plant hydroalcoholic extract had a mild Antinociceptive Peripheral activity as it decreased abdominal contortions induced by acetic acid and was proved ineffective in the hot plate and formalin tests. It was also suggested in the same study that the mechanism of action of the extract didn't resemble that of morphine. Rather, the analgesia might be due to inhibition of bradykinin, prostanoids and other pain mediators [30].

PHYTOCHEMISTRY

Achillea genera, famous for their essential oils, mostly contains terpenes from mono to sesquiterpenes, lignanes, flavonoids [31]. In the aerial parts of *Achillea milefolium*, achilleine, achimillic acids A, B and C, azulene and chamazulene 1,8-cineole and flavonoids such as apigenin and luteolin have been isolated [32] (Table **1**).

MEDICINAL IMPORTANCE

Achillea millefolium L. is used as astringent, lithotripsic agent and antimicrobial and is an antiseptic to urinary infections. It is diaphoretic, antihypertensive, cholagogue, spasmolytic, antispasmodic and it is used topically for wounds and as anti edema and anti-inflammatory while orally for fever, common cold, digestive and carminative. Its use has been documented in varicose ulcer, cuts and injuries. It is also found very effective in leucorrhoea and all kinds of piles [2-6].

COMMERCIAL VALUE

Yarrow yields aromatic flowers with very pleasant, soothing calming and flowery smell. White or pink petals one seeded small flowers are famous for the essential oils they contain in their seeds. The essential oil and flowers are not just aromatic rather they are renowned for their other medicinal properties such as antiseptic, antimicrobial, anti-inflammatory and cleansing agent for which they are of high demand in the cosmetic industry to be used in skin and hair preparations. It promotes healing and cleansing therefore dried flowers are hair care agent and its topical application is beneficial in acnes and improve complexion. It is also tested in a mouthwash for its promising properties. In a clinical safety study, the concentration of *Achillea millefolium* extract in 2%, used in cosmetics, was found non-irritating and safe for use in cosmetics. Commercially, it is available by the brand name of analgesic drug. Moreover, Milfoil is included in several pharmacopoeias and is used commercially in the preparation of a variety of pharmaceutical preparations including teas, tinctures, liquid extracts and also in compound herbal preparations [6, 30, 33, 34].

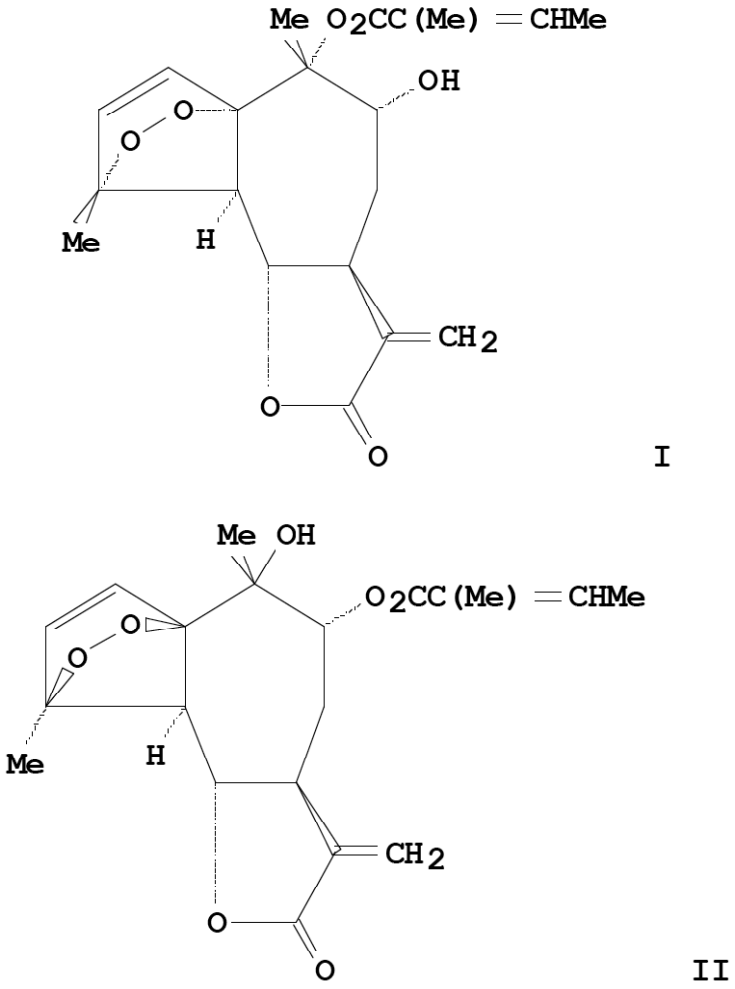

Figure 3: Structure of α-peroxyachifolid (**i**) and β-peroxyisoachifolid (**II**).

TOXICOLOGY

Insecticidal Activity

Ethylacetate extract of leaves and essential oil of *Achillea millefolium* has been tested to be used as mosquito repellent to prevent and control the spread of malaria [35, 36]. Its essential oils was found to have significant insecticidal and fumigant activity against pulse beetle *Callosobruchus maculatus* (F.) on *Vigna radiata* seeds [37]. In addition, in a search for a natural origin fumigant insecticide, several essential oils, including *Achillea millefolium* were evaluated against *Cadra cautella, an insect called* walker [38]. Moreover, owing to its insecticidal and fungicidal properties, *Achillea millefolium* was used as one of the ingredient in a natural fungicidal and insecticidal formulations [39].

Another study shows that *Achillea millefolium* essential oils was found to possess the same repelling properties as that of DEET (N,N-diethyl-m-toluamide on the tick *Ixodes ricinus L.*[40]. Later, *Achillea millefolium* essential oil was found to possess insecticidal activity against larvae of the *Culicidae mosquito Aedes albopictus*. At higher doses at about 300 ppm it caused significant mortality rates in the range of 98.3% to 100% [36].

Safety

In assessing the chronic toxicity of oral use of *Achillea millefolium*, Wistar rats are treated for 90 days with oral aqueous *Achillea millefolium* extract. No significant signs of treatment related toxicity and histopathologies were seen in this study [32]. LD50 and LD25 of the plant was found at 95% confidence interval against small cabbage *Pieris rapae* L. (Lepidoptera: Pieridae) to be 4.19% and 1.69% respectively [41]. LD50 of the ethanolic extract of the achenes was 41297.51 mg/ml when tested on *Artemia salina* [50].

Table 1: Phytochemicals in *Achillea millefolium*

Str. #	Name	Synonym(s)	Molecular Formula
1	Achimilic acid	3-[(2-Hydroxy-2-methyl-5-oxo-3-cyclopenten-1-ylidene)methyl]-2-methylene-6-oxoheptanoic acid, 9CI	$C_{15}H_{18}O_5$
2	Achimillic acid A		$C_{15}H_{18}O_5$
3	Achimillic acid A; 5*Z*-Isomer	Achimillic acid B	$C_{15}H_{18}O_5$
4	Achimillic acid A; 4-Epimer	Achimillic acid C	$C_{15}H_{18}O_5$
5	Chamazulenecarboxylic acid; (*R*)-form		$C_{15}H_{16}O_2$
6	2,4-Decadienoic acid isobutylamide; (*E*,*E*)-form		$C_{14}H_{25}NO$
7	2,4,8-Decatrienoic acid; (2*E*,4*E*,8*Z*)-form, 2-Methylpropylamide	*N*-Isobutyl-2,4,8-decatrienamide *N*-(2-Methylpropyl)-2,4,8-decatrienamide, 9CI 2,4,8-Decatrienoic acid isobutylamide	$C_{14}H_{23}NO$
8	2,4,6-Decatrienoic acid dehydropiperidide; (2*E*,4*E*,6*Z*)-form		$C_{15}H_{21}NO$
9	2,4,6-Decatrienoic acid dehydropiperidide; (2*E*,4*E*,6*Z*)-form, 8,9-Didehydro	2,4,6,8-Decatetraenoic acid dehydropiperidide	$C_{15}H_{19}NO$
10	3,8-Dihydroxy-1(10),4-germacradien-12,6-olide; (1(10)*E*,3α,4*E*,6α,8 ,11ξ)-form, Di-Ac	Millefin	$C_{19}H_{26}O_6$
11	8,10-Dihydroxy-1,4-guaiadien-12,6-olide; (6α,8α,10β,11β*H*)-form, 8-Ac	Achillicin 8-Acetoxyartabsin	$C_{17}H_{22}O_5$
12	9,10-Dihydroxy-1,3,11(13)-guaiatrien-12,6-olide; (5α,6α,9α,10α*OH*)-form, 9-Tigloyl	Isoachifolidiene	$C_{20}H_{24}O_5$
13	Egelolide; 8-Ac	8-Acetylegelolide 3-Oxaachillicin	$C_{16}H_{20}O_6$
14	Egelolide; 8-Angeloyl	8-Angeloylegelolide 8α-Angeloyloxy-3-oxaartabsin	$C_{19}H_{24}O_6$
15	1,4-Epidioxy-9,10-dihydroxy-2,11(13)-guaiadien-12,6-olide; (1α,4α,5α,6α,9α,10α)-form, 10-Tigloyl	α-Peroxyachifolide	$C_{20}H_{24}O_7$
16	1,4-Epoxy-5-hydroxy-10(14)-germacren-12,6-olide; (1α,4α,5β,6α,11β*H*)-form		$C_{15}H_{22}O_4$
17	Homostachydrine; (*S*)-form		$C_8H_{15}NO_2$
18	4-Hydroxy-1,1-dimethylpyrrolidinium-2-carboxylate; (2*S*,4*R*)-form	Betonicine Achillein	$C_7H_{13}NO_3$
19	8-Hydroxy-1(10),4,11(13)-germacratrien-12,6-olide; (1(10)*E*,4*E*,6α,8α)-form, 11β,13-Dihydro, Ac	Acetylbalchanolide	$C_{17}H_{24}O_4$
20	4-Hydroxy-1(10),11(13)-guaiadien-12,6-olide; (4α,5α,6α)-form, 11β,13-Dihydro	4-Hydroxy-1(10)-guaien-12,6-olide 11,13-Dihydromicheliolide	$C_{15}H_{22}O_3$
21	5-Hydroxymethyl-2-furancarboxaldehyde; Me ether	5-(Methoxymethyl)-2-furancarboxaldehyde 5-Methoxymethylfurfural 2-Formyl-5-methoxymethylfuran	$C_7H_8O_3$
22	8-Hydroxy-2-oxo-1(10),3,11(13)-guaiatrien-12,6-olide; (5α,6α,8α)-form, 11α,13-Dihydro, angeloyl	Badkhyzin Badkysin Badkhysin 8α-Angeloyloxyachillin	$C_{20}H_{24}O_5$
23	8-Hydroxy-2-oxo-1(10),3,11(13)-guaiatrien-12,6-olide; (5α,6α,8α)-form, 11β,13-Dihydro, angeloyl	8α-Angeloyloxyleucodin	$C_{20}H_{24}O_5$
24	3-Longipinen-5-one	1-Oxo-α-longipinene Vulgarone B Longiverbenone Longipinenone	$C_{15}H_{22}O$
25	Millefolide		$C_{15}H_{22}O_3$
26	3-(2-Thienyl)-2-propynal	2-Thiophenepropiolaldehyde, 8CI	C_7H_4OS

27	2,4-Undecadiene-8,10-diynoic acid; (2*E*,4*E*)-form, 2-Methylpropylamide	2,4-Undecadiene-8,10-diynoic acid isobutylamide *N*-(2-Methylpropyl)-2,4-undecadiene-8,10-diynamide	$C_{15}H_{19}NO$
28	2,4-Undecadiene-8,10-diynoic acid; (2*E*,4*E*)-form, 2,3-Didehydropiperidide	2,4-Undecadiene-8,10-diynoic acid 2,3-dehydropiperidide	$C_{16}H_{17}NO$

CLINICAL TRIALS

Traditionally yarrow is being used in the diseases of GIT including spasmodic GIT problems (due to flavonoid content of the plant), liver diseases including hepatobiliary problems, inflammatory conditions. The natural products in the *Achillea millefolium* claimed to have a cholagogue and choleretic effect are dicaffeoylquinic acids. Yarrow extracts and fractions also proved to inhibit an enzyme (human neutrophil elastase) involved in inflammatory processes *in vitro*, thus proving its antiphlogistic properties which has been experienced since long ago [22, 49].

Liver Protective Activity

A clinical trial using a compound preparation that is commonly used in Indian traditional system of medicine, which includes *Achillea millefolium* suggested its use for the liver protective activity. The activity is checked on cirrhotic patients and the concentration of liver enzymes also monitored in the study. Author suggested that the activity was due to its diuretic, anti-inflammatory, antioxidative and immunomodulating potential [42]. In chronic hepatitis the plant was checked on elderly patients [43].

Moreover, in a double blind placebo controlled clinical trial using 31 chronic kidney diseased patients, *Achillea millefolium* flower powder was administered and was found to decrease the plasma nitrates and nitrites level and thus decreased the risk of hemorrhages in such patients [44].

Cosmetology

A double blind study (n = 40, two weeks treatment) testing herbal preparation, using three plant extracts including yarrow, did not support the use of preparation in the treatment of atopic dermatitis [45]. Moreover, in a double blind RCT, *Achillea millefolium* extract when applied on middle aged skin was found to activate the factors which decreased the aging effects on skin [46].

Application for Periodontal Diseases

A mouthwash containing *Achillea millefolium* is found effective against periodontal disease, injuries of oral mucosa and swelling [47]. But, later, another study has been done to test *in vivo* the effect of a mouthwash containing 6.3 mg/ml herbal extract mixture of *Juniperus communis* (juniper), *Urtica dioca* (nettle), *Achillea millefolium* (yarrow); 1:1:1 on plaque and gingivitis on plaque and gingivitis. The results of the study have shown that the mixture of the 3 herbal extracts when used in a mouthrinse has no effect on plaque growth and gingival health [8].

Adult females with primary dysmenorrhea were treated with either *Achillea millefolium* tea bags or placebo tea bags in a double-blind randomized trial and the drug group found to have pain relieved by the phytotherapy [48].

AKNOWLEDGEMENT

I would like to thanks Emmeretus Prof. Dr. Ghazala H. Rizwani, Dept. of Pharmacognosy, University of Karachi.

REFERENCES

[1] Flora of Pakistan at www.tropicos.org/Accessed on May 23rd 2012

[2] Pullaiah T. Encyclopedia of world medicinal plants. Regency Publication, New Delhi, India 2006; 1.

[3] WHO Monograpgh on selected medicinal plants, WHO press, Geneva 2007; 4: 179-190.

[4] Khare CP. Indian medicinal plants. An illustrated dictionary. 2007. Springer, N.Y.

[5] Shinwari ZK, Rehman M, Watanabe T, Yoshikawa T. A Pictorial guide to medicinal plants of Pakistan. 2006. Kohat University of Science and Technology, Kohat, Pakistan.

[6] Amelio, FSD. Botanicals. A phytocosmetic desk reference. CRC Press. 1999: pp 23

[7] Rizvi MA, Saeed A, Zubairy HN. Medicinal plants-history, cultivation and uses. HIASR, Hamdard University, Karachi. 2007. 1 and 13.

[8] Van der Weijden GA, Timmer CJ, Timmerman MF, Reijerse E, Mantel MS, van der Velden U. The effect of herbal extracts in an experimental mouthrinse on established plaque and gingivitis. Journal of clinical periodontology 1998; 25(5): 399-403. https://doi.org/10.1111/j.1600-051X.1998.tb02462.x

[9] Koo H, Hayacibara MF, Schobel BD, Cury JA, Rosalen PL, Park YK, Vacca-Smith AM, Bowen WH. Inhibition of Streptococcus mutans biofilm accumulation and polysaccharide production by apigenin and tt-farnesol. Journal of Antimicrobial Chemotherapy 2003; 52(5): 782-789. https://doi.org/10.1093/jac/dkg449

[10] Kumar VP, Chauhan NS, Padh H, Rajani M. Search for antibacterial and antifungal agents from selected Indian

medicinal plants. Journal of Ethnopharmacology 2006; 107(2): 182-188.
https://doi.org/10.1016/j.jep.2006.03.013

[11] Candan F, Unlu M, Tepe B, Daferera D, Polissiou M, SokmenA, Akpulat H. Antioxidant and antimicrobial activity of the essential oil and methanol extracts of Achillea millefolium subsp. millefolium Afan. (Asteraceae). Journal of Ethnopharmacology 2003; 87(2-3): 215-220.
https://doi.org/10.1016/S0378-8741(03)00149-1

[12] Stojanovic G, Radulovic N, Hashimoto T, Palic R. Invitro antimicrobial activity of extracts of four Achillea species: the composition of Achillea clavennae L. (Asteraceae) extract. Journal of ethnopharmacology 2005; 101(1-3): 185-90.
https://doi.org/10.1016/j.jep.2005.04.026

[13] Romero CD, Chopin SF, Buck G, Martinez E, Garcia M, Bixby L. Antibacterial properties of common herbal remedies of the southwest. Journal of Ethnopharmacology 2005; 99(2): 253-257
https://doi.org/10.1016/j.jep.2005.02.028

[14] Kotan R, Cakir A, Dadasoglu F, Aydin T, Cakmakci R, Ozer H *et al*. Antibacterial activities of essential oils and extracts of Turkish Achillea, Satureja and Thymus species against plant pathogenic bacteria. J Sci Food Agric 2010; 90(1): 145-60.
https://doi.org/10.1002/jsfa.3799

[15] Zheljazkov VD, Astatkie T. Effect of residual distillation water of 15 plants and three plant hormones on Scotch spearmint (Menthaxgracilis Sole). Industrial Crops and Products 2011; 33(3): 704-709.
https://doi.org/10.1016/j.indcrop.2011.01.011

[16] Csupor-Loffler Boglarka, Hajdu Zsuzsanna, Zupko Istvan, Rethy Borbala, Falkay George, Forgo Peter, Hohmann Judit. Antiproliferative effect of flavonoids and sesquiterpenoids from Achillea millefolium. L. on cultured human tumour cell lines. Phytotherapy Research 2009; 23(5): 672-676.
https://doi.org/10.1002/ptr.2697

[17] Lebedev AA, Batakov EA, Kurkin VA, Lebedeva EA, Zapesochnaya GG, Avdeeva EV *et al*. The antioxidative activity of a complex hepatoprotective preparation, silybokhol. Rastitel'nye Resursy 2001; 37(2): 69-75.

[18] Temamogullari F, Hayat A, Baba F. Effects of yarrow extract on wound healing in rabbits. Journal of Animal and Veterinary Advances 2009; 8(6): 1204-1206.

[19] Nilforoushzadeh MA, Shirani-Bidabadi L, Zolfaghari-Baghbaderani A, Saberi S, Siadat AH, Mahmoudi M. Comparison of Thymus vulgaris (Thyme), Achillea millefolium (Yarrow) and propolishydroalcoholic extracts versus systemic glucantime in the treatment of cutaneous leishmaniasis in balb/c mice. Journal of vector borne diseases 2008; 45(4): 301-6.

[20] Noureddini M, Rasta VR. Analgesic Effect of aqueous extract of Achillea millefolium L. on rat's formalin test. Pharmacologyonline 2008; 3: 659-664

[21] Choudhary Muhammad Iqbal, Jalil Saima, Todorova M, Trendafilova A, Mikhova B, Duddeck H, Atta-Ur-Rahman. Inhibitory effect of lactone fractions and individual components from three species of the Achillea millefolium complex of Bulgarian origin on the human neutrophils respiratory burst activity. Natural Product Research, Part B: Bioactive Natural Products 2007; 21(11): 1032-1036.
https://doi.org/10.1080/14786410701369623

[22] Benedek Birgit, Kopp Brigitte Achillea millefolium L. s.l. revisited: recent findings confirm the traditional use. Wiener medizinische Wochenschrift (1946) 2007; 157(13-14): 312-4.

[23] Molokovskii DS. Davydov VV, Khegai MD. Antidiabetic activities of adaptogenic formulations and extns. from medicinal plants. Rastitel'nye Resursy 2002; 38(4): 15-28.

[24] Baggio Cristiane Hatsuko, Otofuji Glaucia de Martini, Garcia Thais Lara Cardoso, Freitas Cristina Setim, Nakashima Tomoe, Torres Luce Maria Brandao *et al*. Antiulcer effect of Achillea millefolium L. extracts. Recent Progress in Medicinal Plants 2006; 15: 235-251.

[25] Roncada T, Vicentini VEP, Mantovani MS. Possible modulating actions of plant extracts on the chromosome breaking activity of MMC and Ara-C in human lymphocytes in vitro. Toxicology in vitro 2004; 18(5): 617-622.
https://doi.org/10.1016/j.tiv.2004.02.007

[26] Jovanovic Marina, Poljacki Mirjana, Duran Verica, Vujanovic Ljuba, Sente Ruza. Stojanovic Slobodan Contact allergy to Compositae plants in patients with atopic dermatitis. Medicinski pregled 2004; 57(5-6): 209-18.
https://doi.org/10.2298/MPNS0406209J

[27] Stingeni L, Agea E, Lisi P, Spinozzi F. T-lymphocyte cytokine profiles in compositae airborne dermatitis. Br J Dermatol 1999; 141(4): 689-93.
https://doi.org/10.1046/j.1365-2133.1999.03108.x

[28] Ruecker Gerhard, Manns Detlef, Breuer Judith. Peroxides as plant constituents. VIII. Guaianolide-peroxides from yarrow, Achillea millefolium L., causing allergic contact dermatitis. Archiv der Pharmazie (Weinheim, Germany) 1991; 324(12): 979-81.

[29] Hausen BM, Breuer J, Weglewski J, Ruecker G. a -Peroxyachifolid and other new sensitizing sesquiterpene lactones from yarrow (Achillea millefolium L., Compositae). Contact Dermatitis 1991; 24(4): 274-80.
https://doi.org/10.1111/j.1600-0536.1991.tb01722.x

[30] Pires JM, Mendes FR, Negri G, Duarte-Almeida JM, Carlini EA. Antinociceptive peripheral effect of Achillea millefolium L. and Artemisia vulgaris L.: both plants known Popularly by brand names of analgesic drugs. Phytotherapy Research 2009; 23(2): 212-219
https://doi.org/10.1002/ptr.2589

[31] Si X, Zhang M, Shi Q, Kiyota H. Chemical constituents of the plants in the genus Achillea. Chemistry & Biodiversity 2006; 3(11): 1163-1180.
https://doi.org/10.1002/cbdv.200690119

[32] Cavalcanti AM, Baggio CH, Freitas CS, Rieck L, Silva de Sousa R, Silva-Santos J *et al*. Safety and antiulcer efficacy studies of Achillea millefolium L. after chronic treatment in Wistar rats. Journal of Ethnopharmacology 2006; 107: 277-284
https://doi.org/10.1016/j.jep.2006.03.011

[33] Anon. Final report on the safety assessment of yarrow (Achillea millefolium) extract. International Journal of Toxicology 2001; 20(Suppl. 2): 79-84.
https://doi.org/10.1080/10915810160233785

[34] Benetis R, Radusiene J, Janulis V. Variability of phenolic compounds in flowers of Achillea millefolium wild populations in Lithuania. Medicina (Kaunas) 2008; 44(10): 775-81.
https://doi.org/10.3390/medicina44100097

[35] Jaenson TGT, Palsson K, Borg-Karlson A. Evaluation of extracts and oils of mosquito (Diptera: Culicidae) repellent plants from Sweden and Guinea-Bissau. Journal of medical entomology 2006; 43(1): 113-9.
https://doi.org/10.1093/jmedent/43.1.113

[36] Conti B, Canale A, Bertoli A, Gozzini F, Pistelli. Essential oil composition and larvicidal activity of six Mediterranean aromatic plants against the mosquito Aedesalbopictus (Diptera: Culicidae). Parasitology research 2010; 107(6): 1455-61.
https://doi.org/10.1007/s00436-010-2018-4

[37] Aziz EE, Abbass MH. Chemical composition and efficiency of five essential oils against the pulse beetle Callosobruchus maculatus (F.) on Vignaradiata seeds. American-Eurasian Journal of Agricultural & Environmental Sciences 2010; 8(4): 411-419.

[38] Sim MJ, Choi D, Ahn Y. Vapor phase toxicity of plant essential oils to Cadracautella (Lepidoptera: Pyralidae). Journal of Economic Entomology 2006; 99(2): 593-598.
https://doi.org/10.1093/jee/99.2.593

[39] Besendorfer T. (Bedo Holding AG, Switz.). Stable nontoxic pesticide composition having fungicidal and insecticidal properties. U.S. Pat Appl Publ 2008; 10 pp.

[40] Thorsell W, Mikiver A, Tunon H. Repelling properties of some plant materials on the tick Ixodesricinus L. Phytomedicine 2006; 13(1-2): 132-134. https://doi.org/10.1016/j.phymed.2004.04.008

[41] Hasheminia SM, Sendi JJ, Jahromi KT, Moharramipour S. The effects of Artemisia annua L. and Achillea millefolium L. crude leaf extracts on the toxicity, development, feeding efficiency and chemical activities of small cabbage Pierisrapae L. (Lepidoptera: Pieridae) Pesticide Biochemistry and Physiology 2011; 99: 244-249. https://doi.org/10.1016/j.pestbp.2010.12.009

[42] Huseini H Fallah, Alavian SM, Heshmat R, Heydari MR, Abolmaali K. The efficacy of Liv-52 on liver cirrhotic patients: a randomized, double-blind, placebo-controlled first approach. Phytomedicine: international journal of phytotherapy and phytopharmacology 2005; 12(9): 619-24. https://doi.org/10.1016/j.phymed.2004.10.003

[43] Harnyk TP The use of preparations of plant origin in treating and rehabilitating elderly patients with chronic hepatitis. Likars'ka sprava / Ministerstvo okhorony zdorov'ia Ukrainy 1999; (7-8): 168-70.

[44] Vahid Sepideh, Dashti-KhavidakiSimin, Ahmadi Farrokhlegha, Amini Mohsen, Salehi Surmaghi Mohammad Hosein Effect of herbal medicine Achillea millefolium on plasma nitrite and nitrate levels in patients with chronic kidney disease: a preliminary study. Iranian journal of kidney diseases 2012; 6(5): 350-4.

[45] Shapira Michael Y, Raphaelovich Yisrael, Gilad Leon, Or Reuven, Dumb Avraham J, Ingber Arieh Treatment of atopic dermatitis with herbal combination of Eleutherococcus, Achillea millefolium, and Lamium album has no advantage over placebo: a double blind, placebo-controlled, randomized trial. Journal of the American Academy of Dermatology 2005; 52(4): 691-3. https://doi.org/10.1016/j.jaad.2003.05.008

[46] Pain S, Altobelli C, Boher A, Cittadini L, Favre-Mercuret M, Gaillard C *et al*. Surface rejuvenating effect of Achillea millefolium extract. International journal of cosmetic science 2011; 33(6): 535-42. https://doi.org/10.1111/j.1468-2494.2011.00667.x

[47] Hodisan Viorica, Suciu Gheorghe. Medicine for treating dental disorders. Institutul de Medicina si Farmacie, Rom. Rom 1984; 2: pp.

[48] Jenabi Ensiyeh, Fereidoony Bita. Effect of Achillea millefolium on Relief of Primary Dysmenorrhea: A Double-Blind Randomized Clinical Trial. Journal of pediatric and adolescent gynecology 2015; 28(5): 402-4. https://doi.org/10.1016/j.jpag.2014.12.008

[49] Yaeesh Sheikh, Jamal Qamar, Khan Arif-Ullah, Gilani Anwarul Hassan Studies on hepatoprotective, antispasmodic and calcium antagonist activities of the aqueous-methanol extract of Achillea millefolium. Phytotherapy research: PTR 2006; 20(7): 546-51.

[50] Karim MA, Sidddiqui AA, Rizwani GH, Khan MF. Toxicity of Hydrastis canadensis, Berberis aristata and Achillea millefolium against brine shrimp (Artemia salina) using dosage mortality curve: A Probit approach. Journal of Basic and Applied Sciences 2015; 11: 1-4. https://doi.org/10.6000/1927-5129.2015.11.09

Received on 25-10-2018 Accepted on 05-11-2018 Published on 24-11-2018