Review Article
AMERICAN JOURNAL OF PHARMACY AND HEALTH RESEARCH
www.ajphr.com
2013, Volume 1, Issue 6
ISSN : 2321–3647(online)

Agrimonia eupatoria Linn. A Traditional Herb and its Scientific Testimony- A Review.

Mohammad Asim Khan,[1*] Anzar Alam,[2] Md. Nazamuddin,[1] S Javed Ali,[2] Md. Qutubuddin[2]

1. PG Scholar, Dept. Of Ilmul Advia (Pharmacology), National Institute of Unani Medicine (NIUM), Kottigepalya Bangalore-560091

2. PG Scholar Dept of Moalajat, NIUM, Bangalore-560091

ABSTRACT

Plants are utilized as remedial agents since time immemorial in both organized (Ayurveda, Unani) & Unorganized (folk, ethnic, inhabitant) form that have been revered for their medicinal value. Traditional system of medicines primarily Unani (Greco Arab) and Ayurveda uses plant as a whole or part of it for healing many ailments. Such as, *A. eupatoria* (Agrimonia/agrimony) is one of the most vital plants found in India which is used for its abiding properties of curing a number of diseases. The herb posses highly therapeutic value especially for treatment of lifestyle diseases such as Diabetes, Hypertension and Obesity, accompanied by low-grade inflammation. Research on medicinal plants is one of the leading areas of research globally. Modern era researches and scientific reports also revalidate its usefulness as imperative medicinal herb. The integral objective of reviewing this manuscript is to bring to lime light the litrarery and scientific validation of Agrimonia eupatoria.

Key words: Agrimonia, Unani Medicine, Traditional Medicine, TherapeuticUses

*Corresponding Author Email: dr.asim651@gmail.com
Received 28 August 2013, Accepted 02 September 2013

Please cite this article in press as: Khan MA. *et al., Agrimonia eupatoria* Linn. A Traditional Herb and its Scientific Testimony- A Review. American Journal of Pharmacy & Health Research 2013.

INTRODUCTION

Agrimonia eupatoria Linn. commonly known as agrimony belong to the family of Rosaceae, a perennial hairy herb; stem erect, leaves pinnate, toothed, with velvety undersides and compound and flowers yellow, in terminal, spike-like racemes. [1] In the plant kingdom, Rosaceae family is pigeonholed with 115 genera and 3200 species out of which 257 species are found in India. [2] The Greek literatures Dioscorides describes it as having inverted fruits, so rough and bristly that they adhere to the clothes when riped. The fruit and herb used both externally and internally as an aromatic astringent. Pliny says "The Eupatoria also a plant under royal patronage (Eupator Mithridates, King of Pontus). The seed taken in wine is a sovereign remedy for dysentery." Agrimonia eupatoria appears to have been known to the Western Arabs under the name of "*Sharjrat-el-Baragith* and *Shaukat-el-Muntineh*," and latterly as Ghafith or Khafil. Ibn Sina and the Estern Arabs and Perssian adopted a Persian plant called Ghafat as representing the Eupatorian of the Greeks, and describe a plant having the foliage of Agrimony but with a long dark blue flower. This plant still sold in the East under the name of Ghafith or Ghafis, and is *Gentiana olivieri Griseb***.** [3]

TAXONOMICAL CLASSIFICATION:

Kingdom: Plantae, **Order**: Rosales, **Family**: Rosaceae, **Subfamily**: Rosoideae, **Tribe**: Sanguisorbeae, **Subtribe**: Agrimoniinae, **Genus**: Agrimonia , Species: *eupatoria*.[4]

VERNACULAR NAMES:

A. eupatoria Linn. has diverse names worldwide as well as Indian sub continent as follows:

Arabic : Hasheesha Shulghafiz, Shajrat-el-baraghis, Shaukat-el-muntined

Urdu : Ghaafis

English: Agrimony, Stickle wrote, Cockleburr, Stickwort

Hindi : Ghaafis

Guajarati: Tiryamau

Persian: Ghafat

French : Agrimoine, Aigremoine, Eupatoire des Grecs, Eupatoire des anciens.

German: Ackermennich, Adermennich, Beerkratu

Greek : Ipatorian

Indochina: Chi hao, Long gia, Long nha thao.

Italian: Agrimonia, Eupatorio de Greci.

Roumanian: Turice,Turilamure.

Russian: Reneinik,Reniashok.

Sanskrirt: Tiryatika, Loadev, Balbhadra

Folk: Belu

Unani: Ghaafis. [1,3,6]

HABITAT AND DISTRIBUTION:

Agrimony likes sun lights and grows on moderate humid and dry soils which is usually found in mountainous areas, predominantly in Temperate Himalayas from Murree to Kashmir at the altitude 3000--10000 ft. Sikkim at the altitude of 7000--10000 ft. Khasia at the altitude of 4000--6000 ft. and to the Mishmi hills west region from the Persia to the Atlantic, Siberia, Java, N. America, Sheeraz and Rome. It also found in India, Arunchal Pradesh, Nagaland and Khasi hill in Meghalaya.[1,6,7,8]

BOTANICAL DESCRIPTION:

The whole plant:

A slim, erect leafy perennial herb. The stem is about 60-90 cm long, scarcely branched.[1,7] The herbs deep green, covered with soft silky hairs and when slightly bruised exhaling a peculiar, but pleasant aromatic odour. The whole plant yields a dye. [3]

Leaves:

Leaves are pinnately compound. Lower leaves 10-18cm; leaflets 6-21 in number coarsely toothed, hairy on both surface very unequal, large ones 5-9 elliptic, ovate or obovate rarely orbicular or minute. 1.3-3.8cm intermixed with a number of much smaller ones. Upper leaves gradually smaller and with few leaflets. Stipules adnate to the base of leafstalk.[1,7]

Flowers:

Flowers very numerous 6.0mm in diameter, yellow in colour and terminal spike-like racemes. Each flower in the axial of a small, 3-cleft bract and with two smaller, 3-tootched bracteoles at the tops it stalk. Calyx-tube top-shaped, grooved, bearing outside its mouth a ring of small, hooked bristles; limb 5-lobed. Petal 5, oblong. Stamen 15, Carpels 2, free, enclosed within the calyx tube; styles thread like protruding; stigmas terminal, dilated; ovule solitary. Achenes 1 or 2, in closed in the hardened bristly calyx crowned with a ring of hooked bristles. [1]

Fruits and Seed:

Fruits pendulous, of 1 or 2 achences in closed in the hardened spinous calyx. Calyx of fruits encircled with a thick whorl of hooked prickles, which attach themselves to anything that comes in their way. Flowers appear in about July and August, soon after the seeds become mature. Each

flower contains two seeds. It is astringent and bitter in taste.[9]

INTERACTIONS:

Excessive dose may interact with anticoagulant, hypertensive and hypertensive therapies. As with other tannin rich herbs, "excessive use" should avoid. In view of the lack of toxicity data, use of agrimony should be avoided during pregnancy and lactation. Reportedly affect the menstrual cycle. [10]

MACROSCOPIC (MARKET SAMPLE):

Green pieces of toothed, hairly leaflets, the under surface light in colour, supper dark covered with soft, hooked spines, stem pieces collapsed, wrinkled, green-brown stroaked red covered with coarse hairs.[11]

MICROSCOPY:

Lamina show trichomes, long unicellular, pointed, watery, thick, lignified walls, vessels loose spinal thickening. Glandular trichomes, ovoid heads of 2 to 4 cells, on bent stalks of 1 to 3 cells. Leaf epidermal cells with sinuous anticlinal wall. Stomata anomocytic large, sunken, on lower epidermis. Calcium oxalate prisms occur in the mesophyll. [11]

Active constituents:

Contain volatile oil, bitter principle, colour matter, Tannins.

Phytochmicals constants:

Total Ash	:	Not more than 10%
Acid Insoluble Ash	:	Not more than 2%
Water Soluble Extractive	:	Not less than 12%[11]

PHYTOCHEMICAL STUDIES:

The pharmacological and therapeutic action of vegetable drug depends on their chemical constituents present in that plant. Therefore a detailed survey of literature and chemical abstracts concerning with the chemical composition of the plant has been made and is summarised below:--The plant contains 4.75% Tannin, a fragrant yellow volatile oil, a bitter principle, and yellow colouring matter, which has been used as a dye. [3] Agrimonia eupatoria reported to possess different types of chemical constituents present in the aerial part of the flowering plant contained tannin up to 80%, polysaccharides 19.5%, 2 coumarine substances, 5 flavonoids. Acid hydrolysis of flavonoids yielded the aglycons luteolin, apigenin, qurecetine and the flavonoids glycosides luteolin-7-O-glucoside and apigenin-7-O-glucoside, quercetin-3-rhamnoside and quercetin-3-galactoside Agrimonia eupatoria contains homoprotocatechuic, protocatechuic, caffeic, gentisic,

p-hydroxy benzoic, p-coumeric, vanillic, ferulic and salicylic acids. [6, 7,9,12,13] An astringent property of the plant is due to the presence of a large amount of tannins and small amount of vit.K.[7,14] The plant contains ellagic acid quercitrin, rutin, and chlorogenic acid. Ursolicmacid, a triterpenes, leucoanthocyanins. The presence of kaempferide, kaempferol and their derivatives, such as kaempferol 3-glucoside, kaempferol 3-rhamnoside and kaempferol 3-rutinoside, have also been reported. [15,16] The HPLC profile recorded at 280 nm of the ethyl acetate fraction. Absorption spectra obtained with the diode array detector allowed most peaks to be identified as polyphenols, i.e. flavan-3-ols, flavonols (kaempferol and quercetin derivatives), flavones and phenolic acids.[15] In order to characterize the flavan-3-ols present in the Agrimonia eupatoria L. ethyl acetate fraction, HPLC-MS chromatograms for the molecular ions [M+H] + at m/z 291, 579, 867 and 1155 were recorded. Spectral and chromatographic (retention time) characteristics of the detected flavan-3-ols are included. Compound identification was based on their mass spectra (molecular ion and fragmentation pattern), chromatographic behaviour (elution order) and comparison with procyanidin standards previously isolated in the laboratory. Protocatechuic acid, Procyanidin dimer B1, Procyanidin dimer B3, Procyanidin trimer, Procyanidin trimer C2, Catechin, Procyanidin trimer EEC, Procyanidin dime, Procyanidin dimer B6, Procy Procyanidin tetramer, Procyanidin trimer, Procyanidin dimer B7, Procyanidin trimer C1, p-Coumaric acid, Apigenin 6-C-glucoside, Quercetin 3-O-galactoside, Quercetin 3-O-glucoside, Kaempferol 3-O-glucoside, Kaempferol 3-O-(6″-O-p- coumaroyl)-glucoside . [15] Polyphenolic profile characterization of *Agrimonia eupatoria* L. by HPLC with different detection devices. Liquid chromatography coupled to diode array and electrospray ionization mass spectrometry detection was used to establish the polyphenolic profile of an ethyl acetate fraction from *Agrimonia eupatoria* L. aqueous-alcoholic extract. Additionally, an HPLC technique with post-column derivatization by *p*-dimethylaminocinnamaldehyde was employed for the selective detection and quantification of flavan-3-ols. Important information was obtained by combining the data of these two HPLC techniques. Flavan-3-ols (catechin and procyanidins B1, B2, B3, B6, B7, C1, C2 and epicatechin–epicatechin–catechin), quercetin 3-*O*glucoside, quercetin 3-*O*-galactoside, kaempferol 3-*O*-glucoside, kaempferol 3-*O*-(6″-*O*-*p*-coumaroyl)-glucoside, apigenin 6-*C*glucoside and various phenolic acids were identified. Antioxidant activity of the *Agrimonia eupatoria* L. fraction containing these compounds was assessed through the 1, 1-diphenyl-2-picrylhydrazyl, trolox equivalent antioxidant capacity and thiobarbituric acid reactive substances methods. Significant activity was observed for this fraction, where compounds with recognized anti-inflammatory properties such as procyanidins, kaempferol 3-*O*-(6″-*O*-*p*-coumaroyl)-

glucoside and quercetin glycosides were identified for the first time. These results are predictive of the beneficial effects of this fraction, or some of its compounds, in human health, as possible anti-inflammatory drug.[15] Effect of particle size upon the extent of extraction of antioxidant power from the plants Agrimonia eupatoria, Salvia sp. and Satureja Montana. The dependence of the extent of aqueous extraction of antioxidant compounds on particle size and contact time was studied for three important medicinal plants, that are commonly used in infusions: agrimony, sage and savoury. The effect of extraction time was dependent on the plant considered; however, ca. 5min can be taken as the minimum period required to assure an acceptable degree of extraction of those compounds.[17] A new flavonol glycoside, kaempferide 3-rhamnoside, was isolated from the aerial parts of *Agrimonia eupatoria*. The known compounds kaempferide, kae.[18] Phytochemical studies on an agrimony hydro-alcoholic extract and a polyphenol-enriched fraction obtained from it were carried out. The fraction was found to possess a high concentration of flavan-3-ols, flavonols, flavones and phenolic acids. So, the main purpose of this study was to search out, the extract and fraction antioxidant potential and scavenging activity against the reactive species formed during inflammation and to establish a relationship between such activity and the phenolic composition. Results showed that both the extract and the fraction promptly reacted with DPPH denoting a general radical scavenger activity and a potential antioxidant capacity. They also reacted with superoxideanion, peroxyl and hydroxyl radicals as well as with the oxidant species, hydrogen peroxide,hypochlorous acid and peroxynitrite, strengthening their radical scavenger and antioxidant activities. [19]

THERAPEUTIC USES AS PROVED BY MODERN SCIENTIFIC STUDIES:

Antioxidant and Anti-inflammatory:

Water extract of *A. eupatoria* have found that antioxidant activity. It is due to high polyphenolic content, and the extracts modified the expression of pro-inflammatory factors and enzymes from glutathione metabolism in cell culture and animal models. It also reported that a group of Bulgarian researchers have studied, spectrometically, the antioxidant compounds, such as phenols, in traditionally local plants they found agrimony, prepared as an infusion, among the highest in antioxidant potential. It is believed that phenols are responsible for the antioxidant properties in teas such as mate, black, and green tea. Another group, from Portugal, released similar findings regarding the antioxidant and anti-inflammatory action of the alcohol extract of the plant. A group in Scotland have discovered the free radical scavenging compounds in its seeds. The Effect of *in vitro* digestion upon the antioxidant capacity of aqueous extracts of *Agrimonia eupatoria*, *Rubus idaeus*, *Salvia* sp. And *Satureja montana*. An *in vitro* digestion/

Caco-2 cell culture model was used to assess the stability and bioavailability of phenolic compounds in aqueous extracts of four herbal infusions. Alterations in antioxidant power were monitored by $ABTS^{\bullet+}$, whereas the profile of phenolic compounds was ascertained by HPLC-DAD. The bioavailability of rut in an important flavonoids present in such extracts, and thus a representative of those compounds, was assessed across Caco-2 cells via LC–MS/MS. Our results indicate that several antioxidant compounds are not affected by the (simulated) digestive process, whereas others undergo decreases in their activity throughout said process; a few have their antioxidant capacity hampered under stomach-like conditions. It was also found that rut in can be transported across the Caco-2 cell barrier. [1,6,7,10, 20,21,22,23,24,25]

Anticancer activity:

Cytotoxic effects of Agrimonia eupatoria L. against cancer cell lines in vitro.The results revealed that the five concentrations of plant extracts showed anti-tumor properties in a concentration-dependent manner, and the methanol extract recorded better values of percentage of growth inhibition (PGI) than aqueous extract in HeLa and RD cell lines, while, less PGI values were recorded in the MEF cells. Among these concentrations, 96.0 lg/ml was the most effective in producing PGI in RD and HeLa cancer cell lines for the three investigated time periods.[26]

Anti-hyperglycaemic activity:

The capacity of *A. eupatoria* to lower blood glucose was demonstrated in scientific studies with mice in which diabetes was induced through treatment with an antibiotic called streptozoticin.

Another study reported that aqueous extract of agrimonia shows insulin releasing and insulin like activity in experimental model of Type -1 Diabetes. There is confirmation that diabetes Type-2 Diabetes is supported by low-grade inflammation and immune system activation, underlying insulin resistance.[10, 20,27,28,29,30]

Hepatoprotective activity:

Water extract of A. eupatoria is reported to possess hepatoprotective effects against chronic ethanol-induced liver injury.[31]

Effect of Neuroprotective Flavonoids of Agrimonia eupatoria on Glutamate-Induced Oxidative Injury to HT22 Hippocampal Cells. A methanolic extract of Agrimonia eupatoria (Rosaceae) significantly attenuated glutamate-induced oxidative stress in HT22 hippocampal cells. A new flavonoid, characterized as kaempferol 3-O--D-(200 -O- acetyl-600 -(E)-p coumaroyl)-glucopyranoside (200 -acetyl-tiliroside (1), was isolated from the methanolic extract of A. eupatoria stems together with nine known flavonoids. Compounds 4, 7, 8 and 9 all showed a neuroprotective effect on glutamate-induced toxicity in HT22 cells. [32] Aqueous extract

of *Agrimonia eupatoria* Linn. Inhibition of HBs Ag release against hepatitis B virus (HBV) was investigated from the aerial parts (stems and leaves) of *Agrimonia eupatoria*. [33]

The antioxidant activity of *Agrimonia eupatoria* (Agrimony) and *Agrimonia procera* (Fragrant agrimony) extracts was assessed by measuring in DPPH$^{\bullet}$ radical scavenging and ABTS$^{\bullet+}$ radical decolourisation reaction systems. Radical scavenging capacity of agrimony extracts varied in a wide range (9.1−97.5% in DPPH$^{\bullet}$ reaction and 6.7−79.5% in ABTS reaction) depending on the polarity of the solvent used to obtain the extract. [34]The Effect of particle size upon the extent of extraction of antioxidant power from the plants *Agrimonia eupatoria*, *Salvia* sp. and *Satureja montana* The dependence of the extent of aqueous extraction of antioxidant compounds on particle size and contact time was studied for three important medicinal plants, that are commonly used in infusions: agrimony, sage and savoury. The effect of extraction time was dependent on the plant considered; however, ca. 5 min can be taken as the minimum period required assuring an acceptable degree of extraction of those compounds. As expected, a smaller particle size led to a higher extraction extents; a typical value of 0.2 mm is accordingly recommended. Chlorogenic acid was the dominant phenolic compound extracted from agrimony, whereas caffeic acid dominated in the case of sage or savoury.[25] A group of Korean researchers have used aqueous extracts at varying temperatures from leaves and stems against the Hepatitis B virus. They found that the 60 degrees Celsius temperature of the infusion was the most effective in inhibiting the virus. Also, they found that the plant obtained in mid-July has the highest inhibitory effect. Two other species, Agrimonia: A. pilosa and A. coreana pilosella had the same inhibitory action on the Hepatitis B virus. [1, 7,20, 35]

Anti-bacterial activity:

The anti-fungal and anti-bacterial activity deals with the study of the essential oil of Agrimonia eupatoria Linn. of Kumaon region. The action of essential oil has been studied against the bacteria like *Bacillus subtilis*. Whereas aqueous extract inhibited the growth of *Mycobacterium tuberculosis.*[10] and those strain which are resistant to streptomycin and p-aminosalicylate.[6,7] Staphaureus, E. Coli and the fungus microsporon and tricophyton. The essential oil of the plant is found sensitive against Bacillus subtilis and less sensitive against staphylococcus aureus and E.coli. The essential oil and its constituents did not show any remarkable sensitivity to the fungi Trycophyton and microsporon. [9,36,37]

Uricosuric activity:

The property of promoting the excretion of excess blood uric acid was determined by an Italian group. This explains the traditional uses of a decoction in oil to heal gout, which is a condition

partly, caused accumulation of uric acid.[10,20,,38]

Anti-Diarrhoeal Activity:

This traditional use, which is justified in the light of the high tannin content and the resulting astringent action, is the one for which the plant is recommended by the most widely cited European scientific authority on herbs, the so-called Commission E.[1,7,10,20]

Antipyretic activity:

The Agrimony is said to have been used in fever conditions by the American and Canadian Indians.[10,20]

Skin Irritation and Sores:

This is another of the German Commission E approved remedy for Agrimony. The plant also has a traditional record of use for clearing the skin of eruptions and pimples. The ancient Greeks used the herb as a treatment for serpent bites.[20, 38]

Varicose Veins:

On account if its astringent action, when a fomentation from the plant is applied topically, it soothes inflamed veins (varicose veins).[10,20]

Antiviral activity:

Ethanolic extract of the plant is reported to be active against *Columbia SK virus*. Antiviral activity of plant was tested against *Colombia SK virus* in the mice. The alcoholic extract of Agrimonia eupatoria Linn. were active against the virus.[6,7,] Coumarins interact with anticoagulants, and drugs that increase the risk of bleeding Furanocoumarin contents increase photosensitivity.[6]

Respiratory system:

It is still used in Europe as a popular astringent and stimulant in gargles for sore-throat and horsiness. Respiratory conditions involving mucous-damp / heat, such as bronchitis, asthma, tuberculosis.[1, 3, 6,35,38]

Urinary system:

An astringents and mild bitter, it is valuable remedy for cystitis and urinary incontinence, and has also been used for kidney stones. For relief of pain from gallstones, kidney stones, nephralgia, and general irritation of the urinary organs (Wood, 1997). Used for urinary complaints such as enuresis, urinary incontinence and cystitis (Hoffmann, 2003).[1, 6,7, 8,35,38]

Digestive system:

As a digestive remedy where astringency is needed such as in the case of diarrhoea, acidity, indigestion, IBS with alternating bowel habit (Bartram, 1998).[35]

CONCLUSION:

It is obvious that the medicinal plants are extensively used by the different traditional medical practitioners for curing various ailments in their every day practice. *Agrimonia eupatoria* has been used by physicians of traditional medicine of its various medicinal activities ,modern scientific reports revalidates the claim of traditional medicine scholars by exploring its medicinal properties and further researches are needed for exploring other useful properties of the herb.

Funding: Nil

Conflict of interest: There is no conflict of interest.

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