



Antiinflammatory, Analgesic and Antimicrobial Activities of classical Unani formulation *Raughan-e-Haft Barg*: A Review

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Abstract

Topical drug administration is a localized drug delivery system anywhere in the body mainly through skin, partly from ophthalmic, rectal, and vaginal as topical routes. Unani drug dosage forms (UDDFs), namely *Marham* (Ointment), *Raughan* (Medicated Oil), *Tila* (Liniment) etc. devised and developed exclusively for the local application, *Raughan-e-Haft Barg* is one of the most potent topically used Unani formulation for the management of inflammatory conditions of joint disorders/diseases since long time as it has combination of anti-inflammatory and analgesic properties. It has also been mentioned that the composition of Unani formulation *Raughan-e-Haft Barg* i.e. Aak (*Calotropis procera*), Bakayan (*Melia azedarach*), Bed Anjeer (*Ricinus communis*), Dhatura (*Datura stramonium*), Sanbhaloo (*Vitex negundo*), Sahajna (*Moringa oleifera*), Thuhar (*Euphorbia neriifolia*) and Kunjad (*Sesamum indicum*) possess potent *Muhallil-i-Auram* (antiinflammatory) and *Musakkin* (analgesic) activities in almost all Unani *Qarabadeen* (Unani Pharmacopoeias). In this paper, an attempt has been made to review antiinflammatory, analgesic and antimicrobial activities for a comprehensive understanding of the importance of *Raughan-e- Haft Barg*.

Keywords

Analgesic; Antiinflammatory; *Qarabadeen*; *Raughan*; Topical

INTRODUCTION

Raughan (Medicated Oil) is a medium which is used in different forms. It is used for making the medicine, as medicine itself, as one of the ingredients in a formula or as medicated oil by mixing with other drugs of plant, animal, or mineral origin. It is mostly used as a base (as in the case of ointment) and is generally obtained from plant sources. Oil can be

extracted from different parts of the plant, viz. *Maghziyat* (Kernels of the fruits), *Beekh* (Roots), *Barg* (Leaves), *Gul* (Flowers), *Tukhm* (Seeds) and so on. Based on its use, method of extraction and preparation, it is broadly classified into two main categories: 1. Oil extracted from plant sources for use – Extracted oil. 2. Oil made from mixing with other medicinal drugs (plant, animal or mineral) for

use – Medicated oil. Extraction of oil from plant sources is generally done by the methods given in the Unani texts like *Jal Jantar*, *Patal Jantar*, etc. But because of the increasing demand and large-scale preparation of Unani drugs, manufacturers are now extracting oil by adopting modern technologies. Now days, oil is mostly extracted and obtained by Mechanical Process viz. (i) Cold Expelling Process. (ii) Steam Distillation or Solvent Process. Oil from *Maghziyat* (Kernels) and *Tukhm* (Seeds) are mostly obtained by Cold Expelling Process, while oils from cloves, cinnamon and anise fruits are obtained by Steam Distillation Process. *Raughaniyat* (Extracted and medicated oils) should be preserved in clean and dry glass jar containers under hygienic conditions in cool and dry place and stored for one to two years.

The composition of Raughan-e-Haft Barg is as follows:

S. no.	Name	Botanical name	Part used	Quantity
1.	<i>Barg-e-Aak</i>	<i>Calotropis procera</i>	Barg (Leaves)	1kg
2.	<i>Barg-e-Bakayan</i>	<i>Melia azedarach</i>	Barg (Leaves)	1kg
3.	<i>Barg-e-Bed Anjeer</i>	<i>Ricinus communis</i>	Barg (Leaves)	1kg
4.	<i>Barg-e-Dhatura</i>	<i>Datura stramonium</i>	Barg (Leaves)	1kg
5.	<i>Barg-e-Sanbhaloo</i>	<i>Vitex negundo</i>	Barg (Leaves)	1kg
6.	<i>Barg-e-Sahajna</i>	<i>Moringa oleifera</i>	Barg (Leaves)	1kg
7.	<i>Barg-e-Thuhar</i>	<i>Euphorbia neriifolia</i>	Barg (Leaves)	1kg
8.	<i>Raughan-e-Kunjad</i>	<i>Sesamum indicum</i>	Seeds' oil	6kg

Method of application: *Raughan-e-Haft Barg* is applied lukewarm and massaged on the affected part [6,2].

Table: Mohallil-e-Auram (anti-inflammatory) and Musakkin-e-Alam (Analgesic)

S.No.	Drug Name	References for Mohallil-e-Auram (Anti-inflammatory) and Musakkin-e-Alam (Analgesic) activities of Raughan-e-Haft Barg ingredients from Classical Unani books.
1.	Aak (<i>Calotropis procera</i>)	Anonymous, 2006; Khan, 1313; Hakeem, 2002; Ghani, YNM. Nabi, 2007; Anonymous, 1992; Kabiruddin, 2000; Kirtikar and Basu, 2005; Anonymous, 2005; Khare, 2007; Khan, 1273; Baitar, 1999; Jurjani, 1878; Ghani, 2010; Khan, 2006 [6,36,24,21,57,3,30,44,5,42,41,14,29,22,40].
2.	Bakayan (<i>Melia azedarach</i>)	Khan,1313; Anonymous,2005; Hakeem,2002; Ghani,ynm; Nabi,2007; Kirtikar and Basu, 2005; Nadkarni,2007; Sharma et al,2005; Ghani,2010; Anonymous ,2006; Khan,2006 [37,5,24,22,57,44,58,71,21,6,39].
3.	Bed Anjeer (<i>Ricinus communis</i>)	Khan, 1313; Anonymous, 2005; Hakeem, 2002; Ghani, YNM; Nabi, 2007; Kirtikar and Basu, 2005; Nadkarni, 2007; Sharma et al., 2005; Arzani, 2009; Ghani, 2010; Anonymous, 2006; Khan, 2006 [37,5,24,22,57,44,58,71,12,6,39].
4.	Dhatura (<i>Datura stramonium</i>)	Baitar, 2006; Anonymous, 2007; Ghani, YNM; Kirtikar and Basu, 2005; Nabi, 2007; Hakeem, 2002; Kabiruddin, 2000; Anonymous, 2005; Ghani, 2010; Anonymous, 2006; Khan, 2006; Khan,1874 [13,7,21,44,57,24,30,5,22,6,39,35].
5.	Sanbhaloo (<i>Vitex negundo</i>)	Anonymous,1997; Ghani,ynm; Hakeem,2002; Kabiruddin, 2000; Anonymous,2008; Anonymous ,2006;Anonymous,2005;Ghani,2010; Khan, 2006 [4,22,24,30,8,6,5,22,39].
6.	Sahajna (<i>Moringa oleifera</i>)	Hakeem,2002; Ghani,ynm; Nabi,2007; Kabiruddin,2000; Kirtikar and Basu,2005; Nadkarni,2007;Anonymous,2005; Ghani,2010; Anonymous,2006; Khan,2006 [24,22,57,30,44,58,5,21,6,39].
7.	Thuhar (<i>Euphorbia neriifolia</i>)	Nabi, 2007; Hakeem, 2002; Kabiruddin, 2000; Khan, 1273; Khan, 1313; Anonymous, 2007; Kirtikar and Basu, 2005; Anonymous, 2006; Jurjani,1878; Anonymous, 2005 Ghani, 2010;Khan, 2006 [57,24,30,41,37,7,44,6,29,5].
8.	Kunjad (<i>Sesamum indicum</i>)	Hakeem, 2002; Ghani, YNM; Nabi, 2007; Kabiruddin, 2000; Kirtikar and Basu, 2005; Baitar, 1999; Masihi, 2008; Anonymous, 2005; Arzani, 2009; Ghani, 2010; Anonymous, 2006; Khan, 2006 [24,22,57,30,44,14,53,5,12,21,6,39].

Scientific research on of ingredients of *Raughan-e-Haft Barg*

Aak (*Calotropis procera*)

Antiinflammatory and Analgesic Studies

- Saba *et al.* (2011)^[63] studied ethanolic extract of the leaf of *Calotropis procera* for its antiinflammatory and analgesic activities. The results showed that ethanolic extract of the leaf of *Calotropis procera* had potent antiinflammatory and analgesic activities.
- The methanolic extract of plant *Calotropis procera* has been reported to exhibit potent antiinflammatory activity against carrageenan induced paw oedema and cotton pellet induced granuloma in albino Wistar rats (Basu *et al.* 1991; Dewan *et al.*, 2000)^[16,18].
- The ethanolic extract of root bark of *Calotropis procera* was investigated for its anti-inflammatory activity at different doses in different animal models. The experimental paradigms used were Complete Freund's Adjuvant (CFA) induced arthritis (chronic inflammation), acetic acid induced vascular permeability model in mice for anti-inflammatory activity. The study result showed that ethanolic extract of root bark of *Calotropis procera* has potent anti-inflammatory activity (Parihar *et al.* 2011)^[59].
- A study carried out with the chloroform fraction of *Calotropis procera* root showed that this structure has potent antiinflammatory activity against the exudative and proliferative phases of inflammation, and presents potential analgesic properties through tests assessing changes induced by acetic acid in rats (Parihar *et al.* 2011)^[59].

Wound Healing Study

- In a study by Sharma *et al.* (2014)^[68], *Calotropis procera* was selected for evaluation of its wound healing potential in guinea pigs. For this purpose, four full thickness excision wounds of 8.0 mm diameter were inflicted on the back of guinea pigs. Topical application of 20 µl of 1.0% sterile solution of the latex of the plant twice daily was followed for 7 days. The latex significantly augmented the healing process by markedly increasing collagen, DNA and protein synthesis and epithelization leading to reduction in wound area. Thus, the result provided a scientific rationale for the traditional use of this plant in the management of wound healing.

Antimicrobial study

- Mann *et al.* (1997)^[52] showed in-vitro antibacterial activity of methanol extract of the leaves against gram negative bacteria such as *Salmonella typhi*, *Pseudomonas fluorescens*, *Pseudomonas aeruginosa* and *Escherichia coli*. The methanol extract of the leaves showed potent antibacterial activities against gram negative bacteria.
- Mainasara *et al.* (2011)^[49] conducted a study on antibacterial activity of *Calotropis procera* using water, methanol and ethanol extracts of fruit and bark against Gram positive and Gram-negative bacteria. The result showed that the drug has antibacterial activity against both Gram positive and Gram-negative bacteria.
- The antimicrobial activities of water, methanol and ethanol extracts were determined by using disc diffusion method. The study shows that plant extracts crude and aqueous, methanolic and ethanolic with antibiotics, provide evidence that *Calotropis procera* extracts has the similar antibacterial activity as these antibiotics against test pathogens i.e. *Salmonella Typhi*, *E.Coli* (Muzammal 2014; Kawo *et al.* 2009)^[56,33].

2. Bakayan (*Melia azedarach*)

Antimicrobial study

- Rhaymah *et al.*, (2006)^[62] studied the antibacterial activity of the crude leaf extract of (methanol, ethanol, dichloromethane, ethyl acetate and aqueous) of *Melia azedarach* against Gram negative and Gram-positive bacterial strains using disk diffusion method. The result show that the extracts of the Bakayan leaves has potent antibacterial activities against Gram negative and Gram-positive bacteria.
- Khan *et al.*, (2011)^[34] studied *Melia azedarach* against eighteen hospital isolated human pathogenic bacterial strains. Petroleum ether, benzene, ethyl acetate, methanol, and aqueous extracts at five different concentrations (1, 2, 5, 10 and 15 mg/ml) were evaluated using disk diffusion method. All extracts showed significant antibacterial activity against tested pathogens.
- In a study carried by Saleem *et al.*, (2008)^[65] cream was prepared by methanol flower extract of *Melia azedarach*. Neomycin was used as a standard drug. The result showed that, extract of *Melia azedarach* flower showed potential in curing rabbits suffering from skin infection produced by *Staphylococcus aureus*. The effect was compared with standard drug neomycin.
- Carpinella *et al.*, (1999)^[17] were studied that the ethanolic extract of leaf, seed and fruit of

Melia azedarach against *Aspergillus flavus*, *Fusarium moniliforme*, *Microsporum canis* and *Candida albicans* fungi. The result of the study showed significant antifungal activity against *Aspergillus flavus*, *Fusarium moniliforme*, *Microsporum canis* and *Candida albicans* had been reported.

Wound healing study

- Vidya *et al.*, (2012) ^[76] studied that wound healing potential of *Melia azedarach* leaves in alloxan induced diabetic rats was carried out, result showed that the topical application of methanol leaf extract of *Melia azedarach* possesses significant wound healing activity in alloxan induced diabetic rats. In this study it has been shown that the topical application of *Melia azedarach* leaf extract encourages wound healing in diabetic rats and its effect was analogous with standard povidone iodine. *Melia azedarach* leaf extract enhanced the wound healing in diabetic rats which may be due to its antimicrobial activity.

3. Bed Anjeer (*Ricinus communis*)

Antiinflammatory Studies

- Jena and Gupta (2012) ^[28] studied the antiinflammatory activities of the leaves and root extract in Wistar albino rats in acute and chronic inflammatory models. The study indicated that the paw edema formation due to sub plantar administration of carrageenan, characterizing the cellular events of acute inflammation. The 250 and 500 mg/kg dose of *Ricinus communis* methanolic leaves extract possess protective effect in prevention of cellular events during edema formation and in all the stages of acute inflammation. The antiinflammatory activity of *Ricinus communis* methanolic extract was due to the presence of flavonoids because the flavonoids have the protective effect against carrageenan-induced paw edema in rats (Saini *et al.* 2013) ^[64]
- In a study by Ladda and Kamthane (2014) ^[47], the effect of petroleum ether extract of root of *Ricinus communis* (150 mg/kg p.o) was investigated against Carrageenan, 5-Hydroxytryptamin, Dextran, Bradykinin and Prostaglandin E induced rat's hind paw edema. The result exhibited significant anti-inflammatory activity.

Wound Healing Study

- Jena and Gupta (2012) ^[28] found that *Ricinus communis* possess wound healing activity due to the active constituent of castor oil which produce antioxidant activity and inhibits lipid per oxidation. The agents inhibit lipid

peroxidation is believed to increase the viability of collagen fibrils by increasing the strength of collagen fibers, increasing the circulation, preventing the cell damage and promoting the DNA synthesis.

Antimicrobial Study

- Poonam and Pratap (2012) ^[60] found that the methanolic and aqueous extract of *Ricinus communis* has antimicrobial activity against four clinical bacterial stain; *Escherichia coli*, *Bacillus subtilis*, *Bacillus cereus*, *Staphylococcus aureus* and two fungal strains; *Candida albicans* and *Candida galabrata* with standard drug tetracycline (10 mg /ml).
- Sharma *et al.* (2013) ^[65] reported that *Ricinus communis* showed good activity against *P. aeruginosa*, *S. aureus*, *K. Pneumonia* and *Proteus vulgaris*. The antimicrobial assay revealed that the methanol and ethyl acetate extracts of leaves of *Ricinus communis* possess good zone of inhibition whereas petroleum ether extract has antimicrobial activity only on higher concentration.
- In a study carried out by Verma *et al.* (2011) ^[75], the antimicrobial activity of various extracts of roots (200mg/ml) of *Ricinus communis* was investigated against pathogenic microorganisms such as *Escherichia coli*, *Staphylococcus aureus*, *Pseudomonas aeruginosa*, *Salmonella typhimurium*, *Proteus vulgaris*, *Bacillus subtilis*, *Candida albicans* and *Aspergillus niger* using well diffusion method. The result showed that *Ricinus communis* has potent antimicrobial activity.

1. *Datura (Datura stramonium)*

Antiinflammatory Study

- Sonika *et al.*, (2010) ^[73] found that the ethanolic extract of *Datura stramonium* leaf has significant antiinflammatory activity against carrageenan induced paw edema in rats. In one experiment, 39.43% inhibition of the edema was observed after 3 hours of oral administration of 200 mg/kg extracts. Maximum activity was observed when the extract was administered in doses of 3-hour intervals. Since the extract of *Datura stramonium* inhibited the carrageenan-induced edema that involves the release of histamine and serotonin in the first phase, the inhibitory effect of the extracts could be partly due to inhibition of mast cell mediator release.

Antimicrobial Studies

- Iranbakhsh *et al.* (2010) ^[26] studied that the effects of methanolic extract from root, stem

and leaf of *Datura stramonium* on the vegetative and generative phases of the growth process of four bacterial strains (*Escherichia coli*, *Pseudomonas aeruginosa*, *Staphylococcus epidermidis* and *Bacillus subtilis*) and four fungi strains (*Fusarium semitectum*, *Fusarium colmorum*, *Ceratocystis ulmi* and *Rhizoctonia solani*). The result showed that the methanol extract from green leaf explant callus had inhibitory effects on the growth of *B. subtilis* and *S. epidermidis* with inhibition zones of 22 and 23mm, respectively.

- A study carried out by Shagal *et al.* (2012) [67] found that ethanol extract has the highest inhibitory activity against *Klebsiella pneumonia* followed by *Staphylococcus aureus*, with the least activity against *Salmonella typhi*. The aqueous extract showed activity on *S. aureus* only, while *Neisseria gonorrhea* was resistant to both extracts.

2. *Sanbhaloo (Vitex negundo)*

Antiinflammatory and analgesic study

- Mahalakshmi *et al.*, (2010) [48] studied that the sub-effective dose of *Vitex negundo* potentiated anti-inflammatory activity of phenyl butazone and ibuprofen significantly in carrageenin induced hind paw oedema and cotton pellet granuloma models. The potentiation of anti-inflammatory activities phenyl butazone and ibuprofen by *Vitex negundo* Linn. indicates that it may be useful as an adjuvant therapy along with standard anti-inflammatory drugs.
- Antiinflammatory, analgesic and antirheumatic activity detailed studies have established anti-inflammatory properties of *Vitex negundo* extracts in acute and sub-acute inflammation. Anti-inflammatory and pain suppressing activities of fresh leaves of the plant are attributed to prostaglandin synthesis inhibition, antihistamine, membrane stabilizing (Telang *et al.*, 1999) [74].

3. *Sahajna (Moringa oleifera)*

Antimicrobial study

- Leaves, roots, bark and seeds of *Moringa oleifera* showed *in vitro* antimicrobial activity against bacteria (*Bacillus cereus*, *Candida albicans*, *Streptococcus faecalis*, *Staphylococcus aureus*, *Staphylococcus epidermidis*, *Bacillus subtilis*, *Shigella shinga*, *Shigella sonnei*, *Pseudomonas aeruginosa*, *E.coli* and *Aspergillus niger*), yeast, dermatophytes and helminthes in a disk diffusion technique. It was also reported that

Moringa oleifera exhibit antifungal activity in both dilution and agar plate methods against *Trichophyton rubrum* and *Trichophyton mentagrophytes*, *Epidermophyton xoccosum*, and *Microsporum canis*, *Fusarium solani* and *Rhizopus solani*. 4-(-L-rhamnopyranosyloxy)benzylisothiocyanate, 4-(-L-rhamnopyranosyloxy) benzyl glucosinolate and Pterygospermin are the responsible chemical constituents responsible for its anti-biotic activity (Misahra *et al.*, 2011; Manikandan *et al.*, 2016) [54,51].

Antiinflammatory and Analgesic study

- Methanolic extract of root bark, aqueous extract of roots, methanolic extract of leaves and flowers as well as ethanolic extract of seeds of *Moringa oleifera* had showed anti-inflammatory activity in carrageenan induced paw edema model. (Misahra *et al.*, 2011) [54].
- Methanolic extract of *Moringa oleifera* root bark showed analgesic activity in Acetic acid induced writhing model in mice (Misahra *et al.*, 2011) [54].

Wound healing study

- Misahra *et al.*, (2011) [54] studied that the aqueous extract of *Moringa oleifera* leaves showed wound healing property on male swiss albino mice. It significantly increases wound closure rate, skin breaking strength, granuloma breaking strength as well as decrease in scar area.

4. *Thuhar (Euphorbia neriifolia)*

Anti-inflammatory and Analgesic Study

- Kalpesh *et al.* (2009) [31] observed the anti-inflammatory and analgesic activity of 70% v/v hydro-alcoholic extract of dried leaves of *Euphorbia neriifolia* by oral administration at dose of 400 mg/kg/day of body weight to healthy albino rats. The hydro-alcoholic extract was also evaluated for analgesic activity using Eddy's hot plate method and tail-flick method in albino rats. It showed significant ($P < 0.05$) reduction in the carrageenan-induced paw edema in rats and analgesic activity evidenced by increase in the reaction time by Eddy's hot plate method and tail-flick method in albino rats. The hydro-alcoholic extract also showed greater antiinflammatory and analgesic effect when compared with the standard drugs, Indomethacin and Diclofenac sodium, respectively. The observation indicated significant ($P < 0.001$) activity of the hydro-alcoholic extract of *Euphorbia neriifolia* in the treatment of inflammation and pain.

Wound Healing Study

- The wound healing effect of aqueous extract of latex was evaluated in guinea pig. The 0.5% and 1% sterile aqueous solution of extract facilitated the healing process as evidenced by increase in tensile strength, DNA content, epithelization, and angiogenesis. The aqueous extract of the latex shows potent wound healing activity. (Rasik *et al.* 1996) [65].

5. Kunjad (*Sesamum indicum*)

Antiinflammatory Study

- The anti-inflammatory activity was assessed on the basis of paw edema inhibition induced by the injection of carrageenan (an edematogenic agent) into the subplantar region of the right hind paw of the rat. The results showed that the sesame oil and *sesamin* inhibited the formation of pleural exudates and the leucocyte migration confirming the anti-inflammatory activity (Monteiro *et al.* 2014) [55].

Wound Healing Study

- Free radicals are generated at the site of injury, which are known to impair the healing process by causing damage to cellular membranes, nucleotides, proteins, and lipids. In this context, several antioxidants, such as curcumin, vitamin E, have been reported to give protection against oxidative damage to tissues. The use of antioxidants has been found to promote wound healing. Sesame oil extract has potential antioxidant activity which helps to prevent oxidative damage and promote the healing process. *Sesamum indicum* seeds and oil both promote wound healing in experimentally induced rats. Gel containing seeds or oil applied topically or administration of seeds or oil orally significantly promoted the breaking strength, wound contraction and period of epithelialization in incision, excision and burn wound models (Fukuda *et al.*, 1986; Kiran *et al.* 2008) [20,43].

Antimicrobial Study

- Sesame is naturally antibacterial for common skin pathogens such as *Staphylococcus* and *Streptococcus*, as well as common skin fungi such as athlete's foot fungus. As a throat gargle, it kills *Streptococcus* and other common cold bacteria. It helps sufferers of psoriasis and dry skin ailments. It is a useful natural ultraviolet protector. In a study, the results revealed that minimum inhibitory concentration (MIC) of sesame oil against *Salmonella typhi* is 10 µl/ml. However, for other organism the MIC values were in the range of 350-500 µl/ml. The sesame oil shows best antimicrobial activity and equal

with standard Kanamycin and it shows highest zone of inhibition against *S. typhi*. It reported that sesame oil is found to have the antibacterial activity against *Streptococcus mutans*, *Lactobacilli acidophilus* and total bacteria (Anand *et al.* 2008; Saleem *et al.* 2011) [1,66]

CONCLUSION

After reviewing *Raughan-e-Haft Barg* and its ingredients in the classical and modern text, it may be said that it has *Muhallil-i-Auram* (Resolvent), *Musakkin-i-Alam* (Analgesic) and wound healing properties. Scientific studies also validate that the ingredients of *Raughan-e-Haft Barg* i.e. Aak (*Calotropis procera*), Bakayan (*Melia azedarach*), Baid injeer (*Ricinus communis*), Dhatura (*Datura stramonium*), Sanbhaloo (*Vitex negundo*), Sahajna (*Moringa oleifera*), Thuhar (*Euphorbia neriifolia*) and Kunjad (*Sesamum indicum*) possess potent *Muhallil-i-Auram* (Antiinflammatory), *Musakkin* (Analgesic) and *Muqawwi-e-Asab* (Nervine Tonic) properties. Apart from above, *Raughan-e-Haft Barg* may also be found beneficial management of inflammatory conditions of joint disorders/diseases like *Waja-ul-Mafasil* (Polyarthritis), *Laqwa* (Facial Palsy), *Falij* (Paralysis) etc. Now a days, when joint disorders/diseases increase day by day, it may be one of the best topically used Unani formulation as a drug of choice for the management of inflammatory conditions of joint disorders/diseases.

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