International Journal of Pharmacology

ISSN 1811-7775

science alert

ansinet
Asian Network for Scientific Information

International Journal of Pharmacology 9 (1): 1-11, 2013
ISSN 1811-7775 / DOI: 10.3923/ijp.2013.1.11

Evidence-based Review of Medicinal Plants Used for the Treatment of Hemorrhoids

[1]Roja Rahimi and [2]Mohammad Abdollahi
[1]Faculty of Traditional Medicine and Pharmaceutical Sciences Research Center,
Tehran University of Medical Sciences, Tehran 1417614411, Iran
[2]Faculty of Pharmacy, Pharmaceutical Sciences Research Center,
Endocrinology and Metabolism Research Institute,
Tehran University of Medical Sciences, Tehran 1417614411, Iran

Abstract: Hemorrhoidal disease is a common problem which is usually not managed properly with pharmacologic interventions and will eventually require surgery. However, there are many medicinal plants that were successfully used for the treatment of hemorrhoids in the traditional and folk medicine of different countries. In this study, these medicinal plants have been reviewed and their mechanism of action and their major chemical constituents responsible for their activities have been assessed individually. Among various herbal medicines, *Aesculus hippocastanum*, *Boswellia* species, *Cissus quadrangularis*, *Euphorbia prostrata*, *Juniperus* species, *Melastoma malabathricum*, *Myrtus communis* and *Verbascum* species have got higher support from scientific evidence. These medicinal plants may exert their beneficial effects in hemorrhoids by their anti-inflammatory, analgesic and venotonic activities. Several chemical constituents were identified in these plants which may be responsible for their pharmacological activities, of which, flavonoids, terpenoids, triterpenes and tannins are the majors.

Key words: Hemorrhoids, medicinal plants, chemical constituents, evidence-based medicine, systematic review

INTRODUCTION

"Hemorrhoids" are vascular cushions with a thick submucosa involving the smooth muscle, connective tissues and blood vessels around the anus. Any enlargement, bleeding and protrusion of these cushions is responsible for pathologic hemorrhoids (Thomson, 1975).

Many elements are involved in development of pathologic changes within the hemorrhoidal cushions such as genetics, dysregulation in evacuation of the feces like constipation or diarrhea, sustained strain due to several diseases or conditions and aging. These issues lead to increased pressure within the submucosal arteriovenous plexus and ultimately contribute to swelling of the cushions, laxity of the supporting connective tissue and protrusion into and through the anal canal (Sneider and Maykel, 2010; Lohsiriwat, 2012). Hemorrhoidal disease is a prevalent difficult, for instance, about one million new cases are detected each year in the United States. The estimate is that 5% of the general population is affected by symptoms from hemorrhoids, with 50% of people over the age of 50 having experienced symptoms related to hemorrhoids at some point in time (Sneider and Maykel, 2010). Current conventional treatment of hemorrhoids includes lifestyle modification, pharmacologic therapies and surgery. Pharmacologic therapies include drugs like calcium dobesilate as a venotonic agent, topical agents containing anesthetics and corticosteroids and physical therapies such as ice and sitz baths (Lohsiriwat, 2012). In the current years, medicinal plants have been considered as potentially effective and more tolerable agents for the treatment of different pathological conditions in the gastrointestinal system from mouth to rectum (Rahimi and Abdollahi, 2012a; Rahimi *et al*., 2009, 2010). The medicinal plants with anti-bleeding, venotonic, anti-inflammatory and antinociceptive activities may be useful for treatment of hemorrhoids. In this study, the medicinal plants with any capacity used for the management of hemorrhoids have been criticized and their possible mechanisms of action and their major chemical constituents responsible for their activities have been appraised.

PLANTS FOR THE TREATMENT OF HEMORRHOIDS

Medicinal plants with antihemorrhagic activity and their possible mechanisms of action and their components responsible for their activity have been discussed below.

Corresponding Author: Mohammad Abdollahi, Faculty of Pharmacy, Pharmaceutical Sciences Research Center, Tehran University of Medical Sciences, Tehran 1417614411, Iran

Table 1-3 show *in vitro*, *in vivo* and clinical studies related to their antihemorrhagic activity, respectively.

***Aesculus hippocastanum* L.:** The seed of *Aesculus hippocastanum* has been used in Europe to treat

Table 1: *In vitro* studies on plants used in TIM for treatment of hemorrhoids

Plant	Part or chemical constituents	Model	Results	Reference
Boswellia species	Boswellic acids	Human neutrophil	Direct inhibition of 5-lipooxygenase	Siemoneit *et al.* (2011)
Cestrum auriculatum, *C. hediundium*	Methanol extract of aerial parts	Guinea pig ileum	Inhibition of prostaglandin E(1)-, E(2)-and ACh-induced contractions	Kawano *et al.* (2009)
Cissus quadrangularis Linn.	Methanol extract of aerial parts	Isolated human umbilical vein	Contraction of vascular smooth muscle	Panthong *et al.* (2007)
Commiphora mukul	Methanol extract of gum resin, its hexane fraction and compounds from this fraction	Cox-1 from ram seminal vesicles and Cox-2 from insect cell lysate	Cox-1 and Cox-2 inhibition by all of these components; compounds with the largest inhibition include a cembrenoid and a guggulusterone	Francis *et al.* (2004)
Phlomis pungens var. *pungens*	Phenylpropanoid glycosides, forsythoside B and alyssonoside and the iridoid glycoside lamiide, isolated from the aerial parts	Isolated rat aorta	Prevention of free radical-induced inhibition of the endothelium-dependent relaxation by phenylpropanoid fraction and iridoid fraction	Ismailoglu *et al.* (2002)

Cox: Cyclooxygenase, ACh: Acetylcholine

Table 2: *In vivo* studies on plants used in TIM for treatment of hemorrhoids

Plant	Part or chemical constituents	Animal species	Animal model (s)	Results	Reference
Boswellia serrata	Boswellic acids	Mouse	Arachidonic acid-induced ear edema	Anti-inflammatory effect	Singh *et al.* (2008)
		Mouse	Croton oil (CO)-induced ear edema	Anti-inflammatory effect	
		Rat	Carrageenan-induced paw edema	Anti-inflammatory effect	
Cestrum auriculatum, *C. hediundium*	Methanol extract of aerial parts	Mouse	Acetic acid-induced abdominal constriction	Analgesic effect	Kawano *et al.* (2009)
Cissus quadrangularis /Linn.	Methanol extract of aerial parts	Mouse and rat	EPP-induced ear edema	Anti-inflammatory effect	Panthong *et al.* (2007)
			Carrageenan-and arachidonic acid-induced Edema	Anti-inflammatory effect	
			Acetic acid-induced abdominal constriction	Analgesic effect	
Commiphora myrrha (*T. Nees*) Engl.	Ethanol extract of resin and its different fractions	Mouse	Formalin test	Antinociceptive effect of ethanol extract and its petroleum ether fraction	Su *et al.* (2011)
			Acetic acid-induced abdominal constriction	Analgesic activity of ethanol extract and its petroleum ether fraction	
			Hot plate	No significant antinociceptive effect	
Commiphora myrrha and *Boswellia carterii*	Aqueous extract of resin	Mouse	Formalin test Hot plate antinociceptive effect	Antinociceptive effect No significant	Su *et al.* (2012)
			Carrageenan-induced paw edema	Anti-inflammatory effect	
			PGE2-induced edema	Anti-inflammatory effect	
Juniperus drupacea, *J. communis* var. *communis*, *J. communis* var. *saxatilis*, *J. oxycedrus oxycedrus*, *J. oxycedrus* subsp. *macrocarpa*	The methanol and aqueous extracts of stem, fruit and leaf	Mouse	Carrageenan-induced paw edema	Anti-inflammatory effect of methanol extracts of fruit and leaves from *J. oxycedrus* subsp. *Oxycedrus* and *J. communis* var. *Saxatilis* subsp.	Akkol *et al.* (2009)
			PGE2-induced edema extracts of fruit and leaves from	Anti-inflammatory effect of methanol *J. oxycedrus* subsp. *Oxycedrus* and *J. communis* var. *Saxatilis*	
			P-Benzoquinone-induced abdominal constriction	Antinociceptive effect of methanol extracts of fruit and leaves from *J. oxycedrus* subsp. *Oxycedrus* and *J. communis* var. *Saxatilis*	
			Hot plate	No significant antinociceptive effect from either of species	
Melastoma malabathricum	Aqueous extract of leaf	Rat	Carrageenan-induced edema	Anti-inflammatory activity	Zakaria *et al.* (2006)
	Pure compounds obtained from N-hexane, ethyl acetat and methanol extracts	Mouse	TPA-induced ear edema glucoside and α-amyrin	The strongest anti-inflammatory activity by kaempferol-3-O-	Susanti *et al.* (2008)
	Ethanol extract of stem bark and leaf	Mouse	Acetic acid-induced abdominal constriction	Antinociceptive activity	Sulaiman *et al.* (2004)
			Hot plate	Antinociceptive activity	
	Methanol extract of leaf	Rat	Incision and excision wound	Wound healing activity by increasing wound contracting ability, wound closure time, tensile strength, original tissue regeneration	Sunilson *et al.*, (2008)

Table 2: Continue

Plant	Part or chemical constituents	Animal species	Animal model (s)	Results	Reference
Myrtus communis	Ethanol extract of aerial parts	Rat	Carrageenan-induced paw edema	No significant anti-inflammatory activity	Al-Hindawi *et al.* (1989)
	Aqueous and ethanol extracts of aerial parts	Mouse	Acetic acid-induced abdominal constriction	Antinociceptive activity	Hosseinzadeh *et al.* (2011)
			Hot plate	Antinociceptive activity	
			Xylene-induced ear edema	Anti-inflammatory activity	
			Cotton pellet	Anti-inflammatory activity	
	Aqueous extract of fruit	Mouse	Carrageenan-induced paw edema	Anti-inflammatory activity	Amira *et al.* (2012)
			TPA-induced ear edema	No significant anti-inflammatory activity	
Onosma species (*O. aucheranum* DC., *O. isauricum* Boiss. and Heldr., *O. sericeum* Willd., *O. tauricum* Pallas ex Willd. var. *brevifolium* DC., *O. tauricum* Pallas ex Willd. var. *tauricum*)	Chloroform and ethanol extracts of root	Mouse	P-Benzoquinone-induced abdominal constriction	Antinociceptive activity of chloroform extracts of *Onosma aucheranum* and *Onosma isauricum* and ethanol extracts of *Onosma isauricum* and *Onosma sericeum* Carrageenan-induced paw edema anti-inflammatory activity of chloroform and ethanol extracts of *Onosma isauricum* and ethanolic extract of *Onosma sericeum*	Tosun *et al.* (2008)
Phlomis lanceolata Boiss.	Methanol extract of aerial parts	Mouse	Carrageenan-induced paw edema	Anti-inflammatory activity	Mohajer *et al.* (2005)
			Formalin test	Antinociceptive activity	
			Acetic acid-induced abdominal constriction	Antinociceptive activity	
P. olivieri Benth., anisodonta Boiss. and *P. persica* Boiss.	Methanol extract of aerial parts	Mouse	Acetic acid-induced abdominal constriction	Antinociceptive activity	Sarkhail *et al.* (2003)
Verbascum lasianthum Boiss.	Methanol and aqueous extracts of flower	Mouse	P-Benzoquinone-induced abdominal constriction	Antinociceptive activity of methanol extract	Kupeli *et al.* (2007a)
			Carrageenan-induced paw edema	Anti-inflammatory activity of methanol extract	
Verbascum mucronatum Lam.	Methanol, chloroform and aqueous extracts of flower	Mouse and rat	P-Benzoquinone-induced abdominal constriction	Antinociceptive activity of aqueous extract	Akdemir *et al.* (2011)
			Carrageenan-induced paw edema	Anti-inflammatory activity of aqueous extract comparable to indomethacin	
			Incision and excision wound	Wound healing activity of aqueous extract	

EPP: Ethyl phenylpropiolate, TPA: 12-O-tetradecanoylphorbol-13-acetate

hemorrhoidal disease (Kucukkurt *et al.*, 2010; Anonymous, 2009). A clinical trial on *A. hippocastanum* confirmed that clinical and endoscopic symptoms after average six days of administration to patients with acute symptomatic hemorrhoids was improved (Pirard *et al.*, 1976). The key active component found in *A. hippocastanum* seed extract is aescin. The aescin is a combination of triterpene saponins existing in two forms of α and β. Of these two forms, β-aescin is the active one. Aesin has anti-inflammatory, venotonic and anti-edematous activities (Sirtori, 2001).

***Boswellia* species:** Gum resins of *Boswellia* species, particularly *B. serrata* Roxb. ex Colebr. and *B. carterii* Birdw. have been used in traditional Iranian medicine for the management of hemorrhoids (Arzani, 2005). There are many reports about the anti-inflammatory action of gum resin and its major constituents, boswellic acids (Siddiqui, 2011; Ammon, 2006). Boswellic acids are pentacyclic triterpenes with anti-inflammatory and anti-cancer activities (Poeckel and Werz, 2006).

***Cestrum* species:** *Cestrum auriculatum* L'Hér. and *C. hediundinum* have been used in Peruvian traditional medicine for treatment of hemorrhoids. These two species have shown *in vivo* analgesic effects and *in vitro* anti-inflammatory activity (Kawano *et al.*, 2009).

***Cissus quadrangularis* Linn.:** The *C. quadrangularis*, a medicinal plant indigenous to Asia and Africa, is used for treatment of hemorrhoids. *C. quadrangularis* demonstrated analgesic, anti-inflammatory and venotonic activities. The analgesic property of *C. quadrangularis* is because of inhibition of some local mediators and nociceptors in charge for pain in central nervous system and likewise anti-inflammatory effects in the peripheral tissue by reduction of the release and synthesis of related mediators, principally prostaglandins (Panthong *et al.*, 2007). Administration of *C. quadrangularis* to patients with hemorrhoids condensed the magnitude of

Table 3: Clinical studies on plants used in TIM for treatment of hemorrhoids

Plant	Part or chemical constituents	Dosage	Study design	No. of patients	Duration of treatment	Result	Reference
Aesculus hippocastanum	Seed extract	Tablets equivalent to 40 mg Aesin three times daily	Double-blind, placebo-controlled	38 (Aesin group)/ 34 (placebo group)	2 months	82% of aesin group reported significant improvement in Symptoms (pain, itching, burning, swelling), compared To 32% in the placebo group; Significantly decreased bleeding in 68% of aescin group compared to 38% of placebo Group; Decreased swelling in 76% of Aescin group compared to 35% of placebo group	Pirard *et al.* (1976)
Cissus quadrangularis Linn.	Aerial parts	2 capsules of 500 mg dry powder twice daily	ND	ND	ND	↓ hemorrhoidal pain, inflammation And size of hemorrhoids	Segsunviriya and Choomprabutra (1989)
Euphorbia prostrata	Ethanol extract of aerial parts	100 mg tablet once daily	Uncontrolled	120	2 weeks	Complete cessation of bleeding in 82% of patients; relief of anal pruritis in 73% of patients complaining Of this symptom; relief of discomfort or Heaviness in the anal canal in 88% of patients complaining of these discomforts	Gupta (2011)
Ginkgo biloba	Leave extract with troxerutin and heptaminol	ND	Uncontrolled	37	ND	Complete or partial relief from symptoms of heaviness, tenesmus, pruritus or rectorrhagia in a majority of the patients	Soullard and Contou (1978)
		2 caps twice daily first week and 2 caps once daily second week	Uncontrolled	45	ND	Benefit seen	Hep *et al.* (2000)
		ND	Uncontrolled	22	1 week	Improvement of bleeding, pain, tenesmus and discharge	Sumboonnanonda and Lertsithichai (2004)
Plantago ovata	Seed husk	7 g day^{-1}	Cross-over randomized Controlled	67	6 weeks	Improvement in symptoms and bowel habit	Webster *et al.* (1978)
Plantago ovata	Seed husk	20 g day^{-1}	Randomized Controlled trial	52	6 weeks	Improvement of symptoms; ↓ prolapse and bleeding	Moesgaard *et al.* (1982)
Plantago ovata	Seed husk	11.6 g day^{-1}	Randomized, placebo-controlled	50	40 days	↓ average number of bleeding episodes in Plantago group vs. Control group ($p < 0.001$); ↓number of congested hemorrhoidal cushions in Plantago group vs. Control group ($p < 0.01$); No change in the degree of prolapse after treatment	Perez-Miranda *et al.* (1996)

hemorrhoids and relieved inflammation and pain (Segsunviriya and Choomprabutra, 1989).

***Commiphora* species:** Gum resins from *Commiphora mukul* (Hook. ex Stocks) Eng. and *C. myrrha* (Nees) Engler. have been used as efficacious plant materials for the treatment of hemorrhoids in traditional Iranian medicine. *C. myrrha* showed anti-inflammatory and antinociceptive activities (Su *et al*., 2011, 2012). Anti-inflammatory activity *C. mukul* was demonstrated *in vitro* (Francis *et al*., 2004). Terpenoids and guggulusteroids from *C. mukul* showed potent anti-inflammatory activity (Francis *et al*., 2004; Kimura *et al*., 2001).

***Euphorbia prostrata* aiton:** A preliminary study showed that *Euphorbia prostrata* can be used for the treatment of grade I and II of hemorrhoids with satisfactory efficacy and safety (Gupta, 2011). The mechanisms of action of this plant in hemorrhoids include an increase in lymphatic drainage, reduction in capillary permeability, improvement of venous tone, protection of capillary bed microcirculation and inhibition of inflammatory reactions. As reported, flavonoids in Euphorbia are robust inhibitors of thromboxane A2, prostaglandin E2 and leukocyte stimulation, relocation and adhesion (MacKay, 2001). Studies with the standardized extract of *E. prostrata*, when administered orally showed an inhibition of both carrageenan-induced paw edema and histamine-induced edema (Singla and Pathak, 1990). Ellagic acid is another major constituent of *E. prostrata* extract and has been reported to suppress the histamine release (Choi and Yan, 2009).

***Ginkgo biloba* L.:** Ginkor-fort®, a commercial product from *Ginkgo biloba* leave extract in combination with troxerutin (a flavonoid) and heptaminol (a vasodilator) showed beneficial effects in patients with hemorrhoids (Sumboonnanonda and Lertsithichai, 2004; Hep *et al*., 2000; Soullard and Contou, 1978). *Ginkgo biloba* may exert their beneficial effects in hemorrhoids by its anti-inflammatory and venoprotective activity (Chan *et al*., 2007).

***Juniperus* species:** Several juniperus species are used as a remedy for hemorrhoids in Turkish folk medicine. Between 5 different species of Juniperus, only methanol extracts of fruit and leaves from *J. oxycedrus* subsp. *oxycedrus* and *J. communis* var. *saxatilis* showed significant antinociceptive and anti-inflammatory activities (Akkol *et al*., 2009). Among different compounds present in Juniperus species, diterpenoids such as hinokiol isolated from *J. polycarpos* was shown to exert anti-inflammatory activity (El-Sayed, 1998). Nevertheless, the active antinociceptive and anti-inflammatory constituents in other *Juniperus* species have not been deliberated yet.

***Melastoma malabathricum* L.:** The powdered leaves and roots have been used to relieve the discomfort of hemorrhoids in Malay folk medicine. The flower has been also used for hemorrhoidal bleeding. The antinociceptive, anti-inflammatory and wound remedial activities of this plant were demonstrated by various *in vivo* studies (Zakaria *et al*., 2006; Susanti *et al*., 2008; Sulaiman *et al*., 2004; Sunilson *et al*., 2008). The reported activities may be attributed to different chemical constituents identified in this plant such as flavonoids and tannins (Joffry *et al*., 2012).

***Myrtus communis* L.:** *Myrtus communis* is a medicinal plant used in traditional Iranian medicine for treatment of hemorrhoids (Aghili, 2009). Anti-inflammatory and antinociceptive activities of *M. communis* have been evaluated in several studies (Al-Hindawi *et al*., 1989; Hosseinzadeh *et al*., 2011; Amira *et al*., 2012). Flavonoids are one of the major components of this plant and may play the chief role in these pharmacological properties of *M. communis* (Montoro *et al*., 2006).

***Onosma* species:** *Onosma* species are used for the treatment of hemorrhoids in Turkish folk medicine. Screening of different Onosma species for their anti-inflammatory and antinociceptive effects demonstrated significant activity of *O. isauricum*, *O. sericeum* and *O. aucheranum* (Tosun *et al*., 2008). Onosmins as flavonoid type compounds in *Onosma* species were found to inhibit lipoxygenase enzyme activity (Ahmad *et al*., 2005). Moreover, in the root barks of several *Onosma* species accumulation of naphthaquinones of alkannin and shikonin derivatives have been reported. These compounds possess significant anti-inflammatory activity (Kundakovic *et al*., 2006; Tanaka *et al*., 1986).

***Phlomis* species:** *Phlomis* species has been used in Spanish folk medicine for treatment of hemorrhoids (Limem-Ben Amor *et al*., 2009). There are some reports on antinociceptive and vascular protective effects of *Phlomis* species (Sarkhail *et al*., 2003; Mohajer *et al*., 2005; Ismailoglu *et al*., 2002). Two phenyl propanoid compounds including forsythoside B and alyssonoside may play the major role in vascular protective activity of this plant (Ismailoglu *et al*., 2002). These species also

contain a considerable amount of flavonoids, which show beneficial effects in treatment of hemorrhoids (Limem-Ben Amor *et al*., 2009).

***Plantago ovata* Forssk:** Results of clinical trials showed the beneficial effects of seed husk from *Plantago ovata* on patients with hemorrhoids (Webster *et al*., 1978; Moesgaard *et al*., 1982; Perez-Miranda *et al*., 1996). The seed husk of *Plantago* can reduce bleeding, improve the symptoms and reduce hemorrhoidal cushions. *Plantago* was also used for posthemorrhoidectomy complications. As reported, treatment of patients with *P. ovata* after open hemorrhoidectomy diminished tenesmus rate, pain and markedly shortened postoperative hospital halt (Kecmanovic *et al*., 2006). *P. ovata* is a bulking laxative and causes softening of stool. It also exerts its beneficial effects by producing fairly large amounts of short-chain fatty acids. Anaerobic fermentation of the soluble non-starch polysaccharides from *Plantago* seed results in the production of the propionate, butyrate and acetate in the intestines. These fatty acids may play a critical role in balancing of normal flora of colon and reducing inflammation of the anorectal region (Anonymous, 2002).

***Verbascum* species:** Different species of *Verbascum* have been used to treat hemorrhoids in traditional Turkish medicine. Aqueous extract of the *V. mucronatum* flower has shown anti-inflammatory, antinociceptive and wound healing activities. Fractionation of this extract demonstrated that iridoid glycosides, especially verbascoside are responsible for these activities (Akdemir *et al*., 2011). Besides *V. mucronatum*, other species of *Verbascum* including *V. latisepalum* and *V. salviifolium*, *V. lasianthum*, *V. pterocalycinum* var. *mutense* and *V. salviifolium* displayed significant antinociceptive and anti-inflammatory activities (Tatli *et al*., 2008a, b; Kupeli *et al*., 2007a). Methanol extract of *V. lasianthum* showed significant anti-inflammatory and antinociceptive activity. Fractionation of these extract leads to isolation of different iridoid glycosides of which, aucubin and ilwensisaponin A were found responsible for the mentioned pharmacological activities (Kupeli *et al*., 2007b).

DISCUSSION

Traditional and folk medicines of different countries are an invaluable source to discovery of effective drugs with lower incidence of side effects in modern medicine (Rahimi *et al*., 2010, 2012; Rahimi and Ardekani, 2013). Many of medicinal plants discussed in this study for the management of hemorrhoids have historical backgrounds in traditional medicine for this application. The medicinal plants can improve the symptoms of hemorrhoids such as pain, bleeding, itching, heaviness and tenesmus, rectal prolapse, number of hemorrhoidal cushions and recurrence and increase the rate of wound healing. Their mechanisms of action include anti-inflammatory, anti-nociceptive, venotonic and venoprotective activities or even stool softening by absorption of water absorption as observed for *Plantago ovata*. As shown in Table 4, different classes of compounds, especially flavonoids, triterpenes, tannins and terpenoids may be responsible for anti-hemorrhoidal activity. The chemical structures of some of the natural compounds which may have a role in treatment of hemorrhoids have been shown in Fig. 1. There are some products from flavonoids in the market; the most popular of them is Daflon, hesperidin in combination with diosmin. A meta-analysis of 14 clinical trials on the use of flavonoids for the treatment of hemorrhoids indicated that flavonoids improve symptoms such as bleeding, persistent pain and itching (Alonso-Coello *et al*., 2006). The exact mechanisms of action of flavonoids remain unclear but the possible ones are refining venous tone, boosting lymphatic drainage, dropping capillary hyperpermeability along with anti-inflammatory activities (Meyer, 1994).

There are several plants in traditional Chinese medicine used for stopping bleeding from hemorrhoids and their efficacy has been supported by some clinical trials; but because their scientific names had not been determined in these papers and only it has been implied in their Chinese names; we could not consider them (Gan *et al*., 2010).

Medicinal plants used for treatment of hemorrhoids can also be used for post-hemorrhoidectomy complications such as pain and bleeding thus reducing the use of chemical analgesics and increasing wound healing rate (Rahimi and Abdollahi, 2012b).

The problem of current medicinal plants in treatment of hemorrhoids is that most of them although have traditional use history but lack enough evidence needed for approval as a new drug in the current time. This means that most of the studies have been *in vitro* or *in vivo* but in a systematic manner and thus there are many gaps in their efficacy and safety profile. So the first recommendation is to complete efficacy and safety profile of these plants and then go through clinical trials to prove their efficacy. In the meantime, mixture of these medicinal

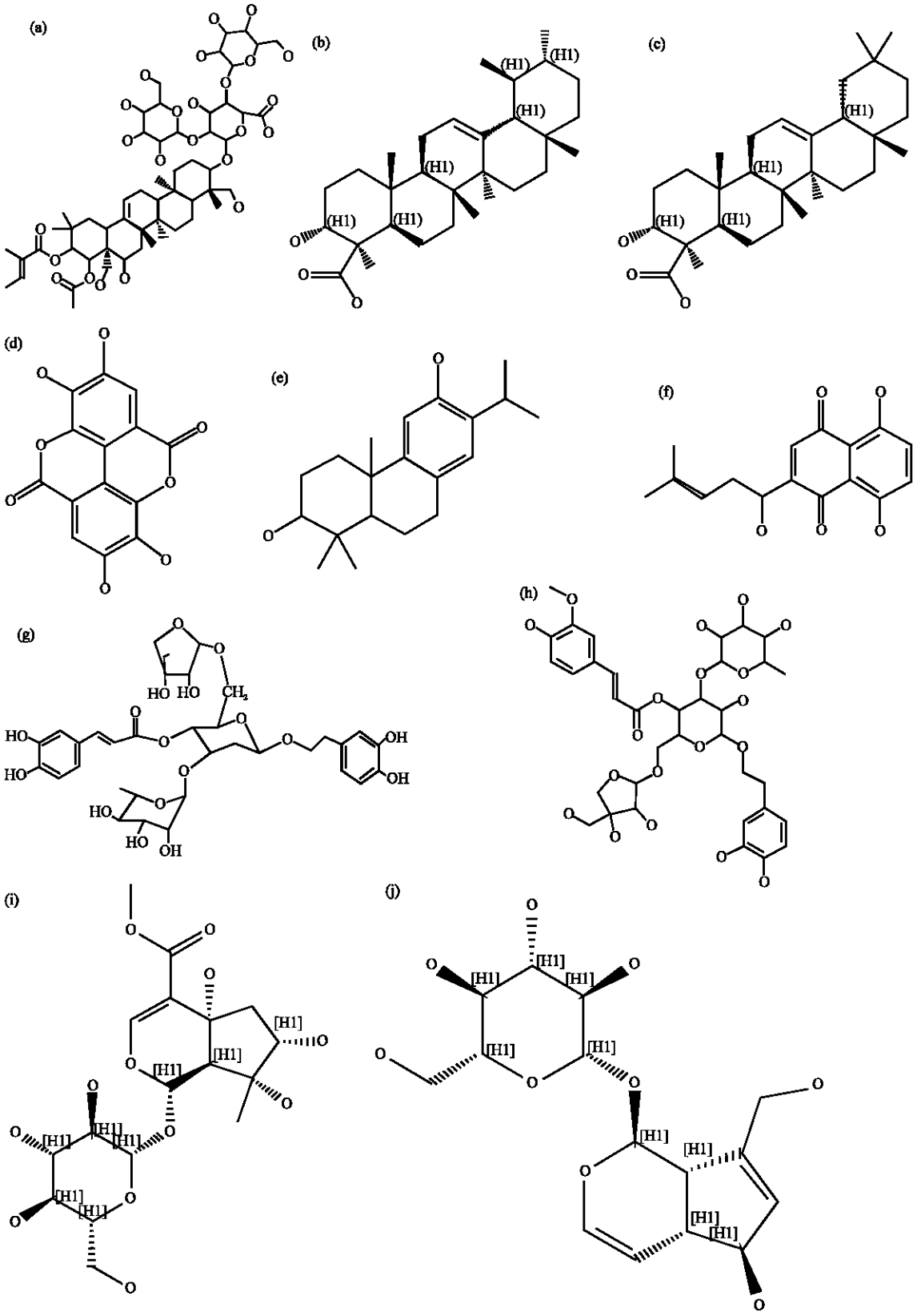

Fig. 1: Continue

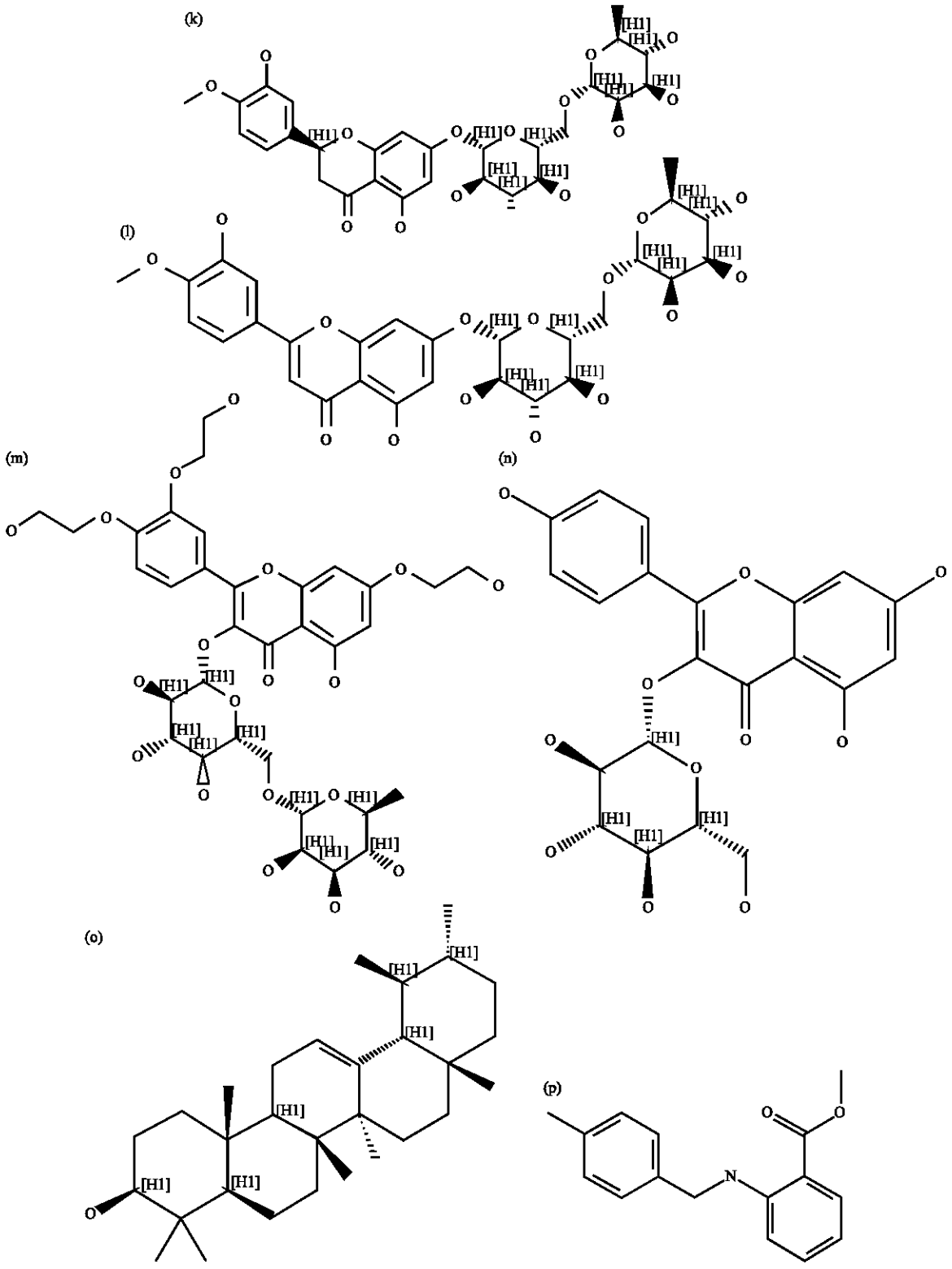

Fig. 1(a-p): Chemical structures of some natural compounds found beneficial in the treatment of hemorrhoids, (a) Aesin, (b) Beta-boswellic acid, (c) Alpha-Boswellic acid, (d) Ellagic acid, (e) Hinokiol, (f) Shikonin, (g) Forsythoside B, (h) Lamiide, (i)Alyssonoside, (j) Aucubin, (k) Hesperidin, (l) Diosmin, (m) Troxerutin (n) Kaempferol-3-glucoside, (o) Alpha-Amyrin and (p) Onosmin B

Table 4: Chemical constituents of medicinal plants responsible for their anti-hemorrhoidal activity

Scientific name of plant	Chemical constituents	References
Aesculus hippocastanum	Triterpene saponins	Sirtori (2001)
Boswellia species	Pentacyclic triterpenes	Poeckel and Werz (2006)
Cestrum species	Indole alkaloids, phenolic compounds	Kawano *et al.* (2009)
Cissus quadrangularis	Flavonoids, triterpenoids, stilbene derivatives	Panthong *et al.* (2007)
Commiphora species	Terpenoids	Su *et al.* (2011)
Euphorbia prostrata	Flavonoids, tannins	Gupta (2011)
Ginkgo biloba	Terpenoids, flavonoids	Chan *et al.* (2007)
Juniperus species	Terpenoids, flavonoids	Akkol *et al.* (2009)
Melastoma malabathricum	Flavonoids, triterpenes, tannins	Joffry *et al.* (2012)
Myrtus communis	Flavonoids	Montoro *et al.* (2006)
Onosma species	Flavonoids, naphthaquinones	Kundakovic *et al.* (2006) and Ahmad *et al.*(2005)
Phlomis species	Phenyl propanoids, flavonoids	Limem-Ben Amor *et al.* (2009) and Ismailoglu *et al.* (2002)
Plantago ovata	Hemicelluloses, polysaccharides	Anonymous (2002)
Verbascum species	Iridoid glycosides	Akdemir *et al.* 2011 and Kupeli *et al.* (2007a)

plants may be more useful by possible synergism that needs to be elucidated. Final notice is that medicinal plants are the valuable source of preparing new drugs for hemorrhoidal disease, but they need to be considered by scientists to go through scientific efficacy and safety tests.

ACKNOWLEDGMENT

Authors acknowledge assistance of Iran National Science Foundation.

REFERENCES

Aghili, M.H., 2009. Makhzan-Al-Advia. Tehran University of Medical Sciences, Tehran, Iran. http://aqlibrary.org/UserFiles/File/makhzan.pdf

Ahmad, I., S.A. Nawaz, N. Afza, A. Malik and I. Fatima *et al.*, 2005. Isolation of onosmins A and B, lipoxygenase inhibitors from *Onosma hispida*. Chem. Pharm. Bull. Tokyo, 53: 907-910.

Akdemir, Z., C. Kahraman, I.I. Tatli, E.K. Akkol, I. Suntar and H. Keles, 2011. Bioassay-guided isolation of anti-inflammatory, antinociceptive and wound healer glycosides from the flowers of *Verbascum mucronatum* Lam. J. Ethnopharmacol., 136: 436-443.

Akkol, E.K., A. Guvenc and E. Yesilada, 2009. A comparative study on the antinociceptive and anti-inflammatory activities of five *Juniperus* taxa. J. Ethnopharmacol., 125: 330-336.

Al-Hindawi, M.K., I.H. Al-Deen, M.H. Nabi and M.H. Ismail, 1989. Anti-inflammatory activity of some Iraqi plants using intact rats. J. Ethnopharmacol., 26: 163-168.

Alonso-Coello, P., Q. Zhou, M.J. Martinez-Zapata, E. Mills, D. Heels-Ansdell, J.F. Johanson and G. Guyatt, 2006. Meta-analysis of flavonoids for the treatment of haemorrhoids. Br. J. Surg., 93: 909-920.

Amira, S., M. Dade, G. Schinella and J.L. Rios, 2012. Anti-inflammatory, anti-oxidant and apoptotic activities of four plant species used in folk medicine in the Mediterranean basin. Pak. J. Pharm. Sci., 25: 65-72.

Ammon, H.P., 2006. Boswellic acid in chronic inflammatory diseases. Planta Med., 72: 1100-1166.

Anonymous, 2002. *Plantago ovata.* (Psyllium). Altern. Med. Rev., 7: 155-159.

Anonymous, 2009. Aesculus hippocastanum (Horse chestnut). Monograph. Altern. Med. Rev., 14: 278-283.

Arzani, M.A., 2005. Tebb-e-akbari. Institute of Medical History, Islamic and Complementary Medicine, Iran University of Medical Sciences, Tehran, pp: 33-40.

Chan, P.C., Q. Xia and P.P. Fu, 2007. *Ginkgo biloba* leave extract: Biological, medicinal, and toxicological effects. J. Environ. Sci. Health., Part C Environ. Carcinog. Ecotoxicol. Rev., 25: 211-244.

Choi, Y.H. and G.H. Yan, 2009. Ellagic Acid attenuates immunoglobulin E-mediated allergic response in mast cells. Biol. Pharm. Bull., 32: 1118-1121.

El-Sayed, A.M., 1998. Diterpene constituents of Juniperus polycarpos and their antimicrobial and anti-inflammatory activities. Zagazig J. Pharma. Sci., 7: 80-86.

Francis, J.A., S.N. Raja and M.G. Nair, 2004. Bioactive terpenoids and guggulusteroids from *Commiphora mukul* gum resin of potential anti-inflammatory interest. Chem. Biodivers., 1: 1842-1853.

Gan, T., Y.D. Liu, Y. Wang and J. Yang, 2010. Traditional chinese medicine herbs for stopping bleeding from haemorrhoids. Cochrane. Database Syst. Rev., Vol. 10.

Gupta, P.J., 2011. The efficacy of *Euphorbia prostrata* in early grades of symptomatic hemorrhoids-a pilot study. Eur. Rev. Med. Pharmacol. Sci., 15: 199-203.

Hep, A., O. Robek and T. Skricka, 2000. Treatment of hemorrhoids from the viewpoint of the gastroenterologist. Personal experience with the Ginkor Fort preparation. Vnitr. Lek., 46: 282-285.

Hosseinzadeh, H., M. Khoshdel and M. Ghorbani, 2011. Antinociceptive, anti-inflammatory effects and acute toxicity of aqueous and ethanolic extracts of *Myrtus communis* L. Aerial parts in mice. J. Acupunct. Meridian. Stud., 4: 242-247.

Ismailoglu, U.B., I. Saracoglu, U.S. Harput and I. Sahin-Erdemli, 2002. Effects of phenylpropanoid and iridoid glycosides on free radical-induced impairment of endothelium-dependent relaxation in rat aortic rings. J. Etnoph., 79: 193-197.

Joffry, S.M., N.J. Yob, M.S. Rofiee, M.M.R.M.M. Affandi and Z. Suhaili *et al*., 2012. *Melastoma malabathricum* (L.) Smith ethnomedicinal uses, chemical constituents and pharmacological properties: A review. Evidence-Based Complementary Altern. Med. 10.1155/2012/258434

Kawano, M., M. Otsuka, K. Umeyama, M. Yamazaki, T. Shiota, M. Satake and E. Okuyama, 2009. Anti-inflammatory and analgesic components from hierba santa a traditional medicine in Peru. J. Nat. Med., 63: 147-158.

Kecmanovic, D.M., M.J. Pavlov, M.S. Ceranic, M.D. Kerkez, V.I. Rankovic and V.P. Masirevic, 2006. Bulk agent Plantago ovata after Milligan-Morgan hemorrhoidectomy with Ligasure. Phytother. Res., 20: 655-658.

Kimura, I., M. Yoshikawa, S. Kobayashi, Y. Sugihara and M. Suzuki *et al*., 2001. New triterpenes, myrrhanol A and myrrhanone A, from *Guggulgum resins* and their potent anti-inflammatory effect on adjuvant-induced air-pouch granuloma of mice. Bioorg. Med. Chem. Lett., 11: 985-989.

Kucukkurt, I., S. Ince, H. Keles, E.K. Akkol, G. Avci, E. Yesilada and E. Bacak, 2010. Beneficial effects of *Aesculus hippocastanum* seed extract on the bodys own antioxidant defense system on subacute administration. J. Ethnopharmacol., 129: 18-22.

Kundakovic, T., N. Fokialakis, S. Dobric, H. Pratsinis, D. Kletsas, N. Kovacevic and I. Chinou, 2006. Evaluation of the anti-inflammatory and cytotoxic activities of naphthazarine derivatives from Onosma leptantha. Phytomedicine, 13: 290-294.

Kupeli, E., I.I. Tatli and Z.S. Akdemir, 2007a. Antinociceptive and anti-inflammatory effects of saponin and iridoid glucosides from Verbascum pterocalycinum var. mutense Hub.-Mor. Z. Naturforsch. C., 62: 813-820.

Kupeli, E., I.I. Tatli, Z.S. Akdemir and E. Yesilada, 2007b. Bioassay-guided isolation of anti-inflammatory and antinociceptive glycoterpenoids from the flowers of *Verbascum lasianthum* Boiss. ex Bentham. J. Ethnopharmacol., 110: 444-450.

Limem-Ben Amor, I., J. Boubaker, M. Ben Sgaier, I. Skandrani and W. Bhouri *et al*., 2009. Phytochemistry and biological activities of Phlomis species. J. Ethnopharmacol., 125: 183-202.

Lohsiriwat, V., 2012. Hemorrhoids: From basic pathophysiology to clinical management. World J. Gastroenterol., 18: 2009-2017.

MacKay, D., 2001. Hemorrhoids and varicose veins: A review of treatment options. Altern. Med. Rev., 6: 126-140.

Meyer, O.C., 1994. Safety and security of Daflon 500 mg in venous insufficiency and in hemorrhoidal disease. Angiology, 45: 579-584.

Moesgaard, F., M.L. Nielsen, J.B. Hansen and J.T. Knudsen, 1982. High-fiber diet reduces bleeding and pain in patients with hemorrhoids: A double-blind trial of Vi-Siblin. Dis. Colon Rectum, 25: 454-456.

Mohajer, M., P. Sarkhail, N. Hajarolasvadi, M.J. Zamani and R. Khorasani *et al*., 2005. Antiinflammatory and analgesic effects of *Phlomis lanceolata* Boiss. and Hohen. extracts and examination of their components. Int. J. Pharmacol., 2: 50-54.

Montoro, P., C.I.G. Tuberoso, S. Piacente, A. Perrone, V. De Feo, P. Cabras and C. Pizza, 2006. Stability and antioxidant activity of polyphenols in extracts of *Myrtus communis* L. berries used for the preparation of myrtle liqueur. J. Pharm. Biomed. Anal., 41: 1614-1619.

Panthong, A., W. Supraditaporn, D. Kanjanapothi, T. Taesotikul and V. Reutrakul, 2007. Analgesic, anti-inflammatory and venotonic effects of *Cissus quadrangularis* Linn. J. Ethnopharmacol., 110: 264-270.

Perez-Miranda, M., A. Gomez-Cedenilla, T. Leon-Colombo, J. Pajares and J. Mate-Jimenez, 1996. Effect of fiber supplements on internal bleeding hemorrhoids. Hepatogastroenterology, 43: 1504-1507.

Pirard, J., P. Gillet, J.M. Guffens and P. Defrance, 1976. Double blind study of Reparil in proctology. Rev. Med. Liege., 31: 343-345.

Poeckel, D. and O. Werz, 2006. Boswellic acids: Biological actions and molecular targets. Curr. Med. Chem., 13: 3359-3369.

Rahimi, R. and M. Abdollahi, 2012a. A systematic review of the topical drugs for post hemorrhoidectomy pain. Int. J. Pharmacol., 8: 628-637.

Rahimi, R. and M. Abdollahi, 2012b. Herbal medicines for the management of irritable bowel syndrome: A comprehensive review. World J. Gastroenterol., 18: 589-600.

Rahimi, R. and M.R. Ardekani, 2013. Medicinal properties of *Foeniculum vulgare* Mill. in traditional Iranian medicine and modern phytotherapy. Chin. J. Integ. Med., 19: 73-79.

Rahimi, R., G. Amin and M.R. Ardekani, 2012. A review on *Citrullus colocynthis* Schrad: From traditional Iranian medicine to modern phytotherapy. J. Altern. Complement. Med., 18: 551-554.

Rahimi, R., M.R. Shams-Ardekani and M. Abdollahi, 2010. A review of the efficacy of traditional Iranian medicine for inflammatory bowel disease. World J. Gastroenterol., 16: 4504-4514.

Rahimi, R., S. Mozaffari and M. Abdollahi, 2009. On the use of herbal medicines in management of inflammatory bowel diseases: A systematic review of animal and human studies. Dig. Dis. Sci., 54: 471-480.

Sarkhail, P., M. Abdollahi and A. Shafiee, 2003. Antinociceptive effect of *Phlomis olivieri* Benth., *Phlomis anisodonta* Boiss. and *Phlomis persica* Boiss. total extracts. Pharmacol. Res., 48: 263-266.

Segsunviriya, C. and S. Choomprabutra, 1989. A clinical study of *Cissus quadrangularis* L. in hemorrhoid patients. Proceedings of the Seminar of Research and Development of Medicinal Plant, Division of Medical Research, Department of Medical Sciences, Ministry of Public Health, Thailand, pp: 54-55

Siddiqui, M.Z., 2011. *Boswellia serrata*, a potential antiinflammatory agent: An overview. Indian J. Pharm. Sci., 73: 255-261.

Siemoneit, U., A. Koeberle, A. Rossi, F. Dehm and M. Verhoff *et al*., 2011. Inhibition of microsomal prostaglandin E2 synthase-1 as a molecular basis for the anti-inflammatory actions of boswellic acids from frankincense. Br. J. Pharmacol., 162: 147-162.

Singh, S., A. Khajuria, S.C. Taneja, R.K. Johri, J. Singh and G.N. Qazi, 2008. Boswellic acids: A leukotriene inhibitor also effective through topical application in inflammatory disorders. Phytomedicine, 15: 400-407.

Singla, A.K. and K. Pathak, 1990. Topical antiinflammatory effects of Euphorbia prostrata on carrageenan-induced footpad oedema in mice. J. Ethnopharmacol., 29: 291-294.

Sirtori, C.R., 2001. Aesin: Pharmacology, pharmacokinetics and therapeutic profile. Pharmacol. Res., 44: 183-193.

Sneider, E.B. and J.A. Maykel, 2010. Diagnosis and management of symptomatic hemorrhoids. Surg. Clin. North Am., 90: 17-32.

Soullard, J. and J.F. Contou, 1978. A study on the use of ginkor in proctology (author's transl). Semaine Hopitaux, 54: 1177-1179.

Su, S., T. Wang, J.A. Duan, W. Zhou and Y.Q. Hua *et al*., 2011. Anti-inflammatory and analgesic activity of different extracts of *Commiphora myrrha*. J. Ethnopharmacol., 134: 251-258.

Su, S., Y. Hua, Y. Wang, W. Gu and W. Zhou *et al*., 2012. Evaluation of the anti-inflammatory and analgesic properties of individual and combined extracts from *Commiphora myrrha* and *Boswellia carterii*. J. Ethnopharmacol., 139: 649-656.

Sulaiman, M.R., M.N. Somchit, D.A. Israf, Z. Ahmad and S. Moin, 2004. Antinociceptive effect of *Melastoma malabathricum* ethanolic extract in mice. Fitoterapia, 75: 667-672.

Sumboonnanonda, K. and P. Lertsithichai, 2004. Clinical study of the *Ginko biloba*-troxerutin-heptaminol Hce in the treatment of acute hemorrhoidal attacks. J. Med. Assoc. Thai., 87: 137-142.

Sunilson, A.J., J. James, J. Thomas, J. Paulraj, V. Rajavel and M.M. Paliniappan, 2008. Antibacterial and wound healing activities of *Melastoma malabathricum* Linn. Afr. J. Infect. Dis., 2: 68-73.

Susanti, D., H.M. Sirat, F. Ahmad and R.M. Ali, 2008a. Bioactive constituents from the leaves of *Melastoma malabathricum* L. J. Ilmiah. Farmasi, 5: 1-8.

Tanaka, S., M. Tajima, M. Tsukada and M. Tabata, 1986. A comparative study on anti-inflammatory activities of the enantiomers, shikonin and alkannin. J. Natural Products, 49: 466-469.

Tatli, I.I., Z.S. Akdemir, E. Yesilada and E. Kupeli, 2008a. Anti-inflammatory and antinociceptive potential of the methanolic extract of *Verbascum salviifolium* Boiss. Z. Naturforsch. C, 3: 196-202.

Tatli, I.I., E.K. Akkol, E. Yesilada and Z.S. Akdemir, 2008b. Antinociceptive and antiinflammatory activity on seven endemic *Verbascum* L. species growing in Turkey. Pharm. Biol., 46: 781-788.

Thomson, W.H., 1975. The nature of haemorrhoids. Br. J. Surg., 62: 542-552.

Tosun, A., E.K. Akkol, O. Bahadir and E. Yesilada, 2008. Evaluation of anti-inflammatory and antinociceptive activities of some *Onosma* L. species growing in Turkey. J. Ethnopharmacol., 120: 378-381.

Webster, D.J., D.C. Gough and J.L. Craven, 1978. The use of bulk evacuant in patients with haemorrhoids. Br. J. Surg., 65: 291-292.

Zakaria, Z.A., R.N.S. Raden Mohd Nor, G. Hanan Kumar, Z.D.F. Abdul Ghani and M.R. Sulaiman *et al*., 2006. Antinociceptive anti-inflammatory and antipyretic properties of *Melastoma malabathricum* leaves aqueous extract in experimental animals. Can. J. Physiol. Pharmacol., 84: 1291-1299.