

# INVESTIGATION OF VASOACTIVE ION CONTENT OF HERBS USED IN HEMORRHOID TREATMENT IN TURKEY

MAHIR GULEC, RECAI OGUR, HÜSAMETTİN GUL\*,  
AHMET KORKMAZ\*\* AND BILAL BAKIR

*Gulhane Medical School, Department of Public Health, Ankara, Turkey*

*\*Gulhane Medical School, Department of Analytical Toxicology, Ankara, Turkey*

*\*\*Gulhane Medical School, Department of Physiology, Ankara, Turkey*

## ABSTRACT

**Objectives:** The aim of the present study is to determine anion and cation contents of the herbals used in Turkish folk remedy to explore the rationale of their use in hemorrhoid treatment in the context of the vasoactivity of these elements.

**Design:** Herbs used in the treatment of hemorrhoid were determined by the way of literature search. These herbs were obtained from certificated herb sellers. Grinded herb samples were placed in individual tubes containing methanol and incubated for 48 hours at 30°C. At the end of the incubation, supernatants were analyzed for their ion concentrations by using ion chromatography.

**Results:** The difference between ion levels between systemic and locally used herbs, was not statistically significant ( $p>0.05$ ). Anion concentrations (except nitrate) of locally used herbs were slightly higher than systemically used herbs ( $p>0.05$ ). Cation levels (except magnesium) of systemically used herbs were slightly higher than locally used herbs ( $p>0.05$ ).

It was shown that the concentration of vasoconstrictor effective ions was higher than the concentration of vasodilator effective ions ( $p<0.001$ ). While vasoconstrictor ion concentration of systemically used herbs was  $88.06 \pm 147.42$ mg, vasodilator ion concentration of locally used herbs was  $90.15 \pm 136.94$ mg. The difference between vasodilator concentrations of groups was more evident;  $5.39 \pm 9.80$  mg and  $14.32 \pm 66.48$  mg for locally and systemically used herbs respectively.

**Conclusions:** This study showed that herbal remedies used for the treatment of hemorrhoid in Turkey contain vasoactive and especially vasoconstrictor ions. Vasoconstrictor agents could amplify each others' effects as it has been previously shown, therefore, it is probable that the vasoconstrictor ion contents could contribute to the curative effects of herbals in the treatment of hemorrhoids.

**Keywords:** Hemorrhoid, vasoactive ions, ion chromatography.

## INTRODUCTION

Hemorrhoids are common conditions of anorectal region (Gupta 2005; MacKay 2001). Besides being one of the most frequent reason of rectal hemorrhages, they may cause pain, discomfort and disability of patient (Gupta 2005; Leff 1987). Conservative therapies for hemorrhoids include diet, lifestyle changes, and hydrotherapy which require a high degree of patient compliance to be effective. When conservative hemorrhoid therapy is ineffective, many physicians may choose other non-surgical modalities: injection sclerotherapy, cryotherapy, manual dilation of the anus, infrared photocoagulation, bipolar diathermy, direct current electrocoagulation, or rubber band ligation (Gupta 2005; Yuksel *et al.* 2008). Injection sclerotherapy is the non-surgical treatment for primary varicose veins (Chew *et al.* 2003; Elram *et al.* 2007). These methods usually require physicians to be specially trained, own specialized equipment, and assume associated risks. Despite the presence of various non-surgical therapies for hemorrhoids, none of these methods

has established superiority over each other (Gupta 2005). If a non-surgical approach fails, the patient is often referred to a surgeon (Gupta 2005; Jacob 1987; MacKay 2001; Smith 1987).

On the other hand, there are herbal remedies for hemorrhoid treatment in almost every culture. Turkey has a rich flora and numerous plants were reported for the treatment of hemorrhoid in Turkish folkloric medicine, also it has been showed that hemorrhoids are one of the main health problems leading to the usage of herbal medication for their treatment (Ogur *et al.* 2006). Some of these herbal medications are used internally as well as some of them are used locally (Baytop 1999; Gürhan *et al.* 2004; Ogur *et al.* 2006).

From pharmacognosic perspective, probably some of chemicals in plants may be effective in hemorrhoid treatment. And also it is obvious that some of these chemicals are complex polyphenolic compounds, but some of the effective constituents of these plants may be vasoactive ions. Although, vasoactivity of several elements is well-known, little is known about the role of

\*Corresponding author: e-mail: recaiogur@yahoo.com

vasoactivity of anions and/or cations in the treatment of hemorrhoids. For example, fluoride is a strong vasoconstrictor anion which exists in various herbals (Jeon *et al.* 2006). Some of the herbals in hemorrhoids are used externally via sitting bath and it is probable that the concentration of anions and cations in the bath is sufficient to produce vasoconstriction which might cause healing hemorrhoids. Therefore, we aimed to investigate the anion and cation contents of the herbals used in Turkish folkloric medicine to explore the rationale of their use in hemorrhoid treatment in the context of the vasoactivity of these ions.

## MATERIALS AND METHODS

Herbs used in the treatment of hemorrhoid were determined by the way of literature search (Baytop 1999; Gürhan and Ezer 2004; Ogur *et al.* 2006). Properties and usage of the herbals used for hemorrhoid treatment in Turkey was shown in table 1. These herbs were obtained from certificated herb sellers. In order to provide exact dryness, all of the herbs were dried for two weeks in a dark and dry room at room temperature. All of the samples were grinded by using a laboratory blender (Waring, Torrington, CT, USA). One gram of grinded herb samples were placed in individual tubes and 10 ml methanol was added into every tube. Lidded tubes were

incubated for 48 hours in a shaking water bath (Nuve BM 302, Ankara, Turkey) at 30°C. At the end of the incubation, samples were centrifuged for 10 minutes at 2500 rpm (Hermle Z200A, Gosheim, Germany), and supernatants were collected by using pipettes. Liquid portions of samples were filtered by using 22 nm injector filters (Sartorius Minisart, Goettingen, Germany). One milliliter of samples was analyzed for their ion concentrations by using ion chromatography (Dionex ICS – 1000, Sunnyvale, CA, USA). For anion and cation analyses separate colons and accessories were used (AS-9 HC, AG-9 HC, CS12A, CG12A, Sunnyvale, CA, USA). Standardized ion mixtures at different concentrations were used for measuring ion quantities of samples. Details of ion chromatography analyses were shown in Table 2. Ion chromatography measures were repeated for three times and their medians were accepted as the ion contents of samples. Results were standardized for 100 grams of dried plant samples (analyses results multiplied by 100 for every ion of samples).

Results were statistically analyzed by using computer software (SPSS for Windows version 11.5, (Chicago, IL, USA)). Non-parametric Mann-Whitney U and independents samples t test were used where appropriate for comparing groups.

**Table 1:** Herbs for the treatment of hemorrhoids and usage

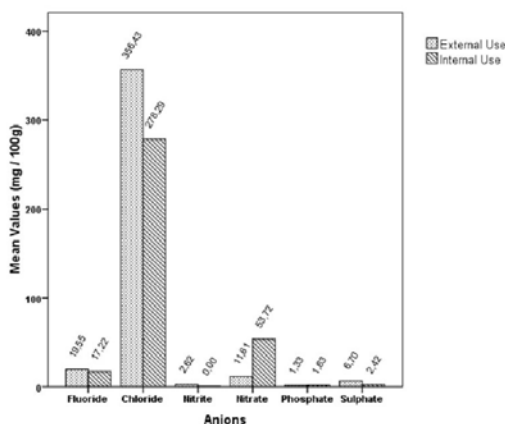
Botanical name	Family	Common name	Turkish name	Usage
<i>Aesculus hippocastanum</i> L.	Sapindaceae	Horse-chestnut	Atkestanesi	Systemic
<i>Allium sativum</i> L.	Alliaceae	Garlic	Sarımsak	Systemic
<i>Cassia angustifolia</i> Vahl.	Fabaceae	Senna	Sinameki	Systemic
<i>Crataegus oxyacantha</i> L.	Rosaceae	Hawthorn (fruit)	Alıç meyvesi	Systemic
<i>Crataegus oxyacantha</i> L.	Rosaceae	Hawthorn (leaves)	Alıç yaprağı	Systemic
<i>Ficus carica</i> L.	Moraceae	Common fig	İncir	Systemic
<i>Fumaria officinalis</i> L.	Papaveraceae	Common Fumitory	Şahtere	Systemic
<i>Galium aparine</i> L.	Rubiaceae	Cleavers	Yoğurtotu	Systemic
<i>Liquidambar orientalis</i> Mill.	Altingiaceae	Turkish Sweetgum	Günlük	Systemic
<i>Malva sylvestris</i> L.	Malvaceae	Common Mallow	Ebegümece	Systemic
<i>Momordica charantia</i> L.	Cucurbitaceae	Bitter melon	Kudret Narı	Systemic
<i>Nigella sativa</i> L.	Ranunculaceae	Blackseed	Çörekotu	Systemic
<i>Peganum harmala</i> L.	Nitrariaceae	Harmal	Üzerlik	Systemic
<i>Silybum marianum</i> L.	Asteraceae	Blessed Milk Thistle	Mübarek diken	Systemic
<i>Symphytum officinale</i> L.	Boraginaceae	Comfrey	Karakafesotu	Systemic
<i>Teucrium chamaedrys</i> L.	Lamiaceae	Wall germander	Kısa Mahmut Otu	Systemic
<i>Zingiber officinale</i> Rosc.	Zingiberaceae	Ginger	Zencefil	Systemic
<i>Achillea millefolium</i> L.	Asteraceae	Common Yarrow	Civanperçemi	Local
<i>Cupressus sempervirens</i> L.	Cupressaceae	Mediterranean Cypress	Servi Kozalağı	Local
<i>Myrtus communis</i> L.	Myrtaceae	Myrtle	Mersin	Local
<i>Rubus caesius</i> L.	Rosaceae	Dewberry	Böğürtlen	Local
<i>Sambucus nigra</i> L.	Adoxaceae	Elderberry	Mürver Çiçeği	Local
<i>Verbascum thapsus</i> L.	Scrophulariaceae	Common Mullein	Sığırkuyruğu	Local

**Table 2:** Ion chromatography conditions

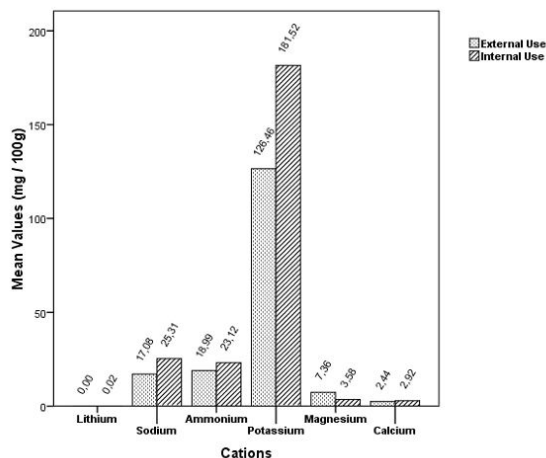
Anion conditions	Data_Collection_Rate = 5.0 [Hz] CellTemperature.Nominal = 35.0 [°C] ColumnTemperature.Nominal = 0.0 [°C] Suppressor_Type = ASRS_4mm ; Pump_ECD.Carbonate = 9,0 Suppressor_Current = 45 [mA] Flow = 1.00 [ml/min] -2.300 Pump_ECD_Relay_1.Closed      Duration=138.00 0.000 Autozero ECD_1.AcqOn Pump_InjectValve.InjectPosition      Duration=120.00 20.000 ECD_1.AcqOff End
Cation conditions	Data_Collection_Rate = 5.0 [Hz] CellTemperature.Nominal = 35.0 [°C] ColumnTemperature.Nominal = 30.0 [°C] Suppressor_Type = CSRS_4mm ; Pump_ECD.MSA = 18,0 Suppressor_Current = 53 [mA] Flow = 1.00 [ml/min] -2.300 Pump_ECD_Relay_1.Closed      Duration=138.00 0.000 Autozero ECD_1.AcqOn Pump_InjectValve.InjectPosition      Duration=120.00 18.000 ECD_1.AcqOff End

## RESULTS

Anion and cation measurement results were shown in table 3. Herbs were grouped for their usage types (systemic or local) and for their activities on vessels. Although there were differences between ion levels between systemically and locally used herbs, these differences were not statistically significant ( $p>0.05$ ). Mean anion and cation concentrations of herbs were shown in figs. 1 and 2.



**Fig. 1:** Anion levels (means) of herbs used for hemorrhoid treatment in Turkey



**Fig. 2:** Cation levels (means) of herbs used for hemorrhoid treatment in Turkey

Nitrite was detected in only one sample (*Sambucus nigra*), and just one herb sample contained lithium (*Crataegus oxyacantha* (leaves)).

It was determined that there was difference among anion and cation levels of herbs when they were grouped by systemic and local usage. Anion concentrations (except nitrate) of locally used herbs were higher than systemically used herbs, but the difference was not statistically significant ( $p>0.05$ ). Cation levels (except

**Table 3:** Ions (mg/100gr dried crude material)

Plants	Anions*						Cations*					
	Fluoride	Chloride	Nitrite	Nitrate	Phosphate	Sulfate	Lithium	Sodium	Ammonium	Potassium	Magnesium	Calcium
Achillea millefolium	15.200	415.190	n.d.	9.804	n.d.	26.62	n.d.	9.660	31.062	127.974	2.956	2.486
Aesculus hippocastanum	16.777	284.288	n.d.	n.d.	n.d.	n.d.	n.d.	13.741	6.151	70.764	1.267	0.873
Allium sativum	1.705	131.408	n.d.	3.418	n.d.	n.d.	n.d.	13.852	51.798	29.174	0.841	1.581
Cassia angustifolia	18.758	260.896	n.d.	n.d.	n.d.	n.d.	n.d.	27.561	17.379	52.691	10.348	2.812
Crataegus oxyacantha (fruit)	42.022	489.510	n.d.	n.d.	16.122	35.948	n.d.	9.552	7.558	71.795	2.912	1.888
Crataegus oxyacantha (leaves)	16.230	217.793	n.d.	n.d.	n.d.	n.d.	0.301	10.464	2.711	44.118	n.d.	2.301
Cupressus sempervirens	9.603	321.900	n.d.	4.244	4.87	4.682	n.d.	18.096	7.952	116.064	0.505	n.d.
Ficus carica	24.716	205.408	n.d.	n.d.	7.168	n.d.	n.d.	42.505	13.824	125.571	2.748	1.763
Fumaria officinalis	1.295	171.968	n.d.	499.9459	n.d.	n.d.	n.d.	16.118	45.007	693.136	11.251	8.924
Galium aparine	28.812	209.848	n.d.	10.998	n.d.	n.d.	n.d.	21.347	8.745	280.188	9.254	16.585
Liquidambar orientalis	24.339	497.424	n.d.	n.d.	n.d.	n.d.	n.d.	0.585	40.348	1.049	n.d.	1.372
Malva sylvestris	18.544	374.806	n.d.	95.818	n.d.	n.d.	n.d.	49.539	29.395	357.536	2.848	1.991
Momordica charantia	30.515	260.048	n.d.	n.d.	n.d.	n.d.	n.d.	12.847	22.528	148.992	4.403	n.d.
Myrtus communis	56.969	547.990	n.d.	n.d.	n.d.	n.d.	n.d.	17.315	9.145	76.752	21.341	6.236
Nigella sativa	15.008	221.640	n.d.	n.d.	n.d.	n.d.	n.d.	13.801	7.568	60.236	1.894	4.304
Peganum harmala	17.600	554.376	n.d.	52.79	n.d.	n.d.	n.d.	148.105	46.931	347.631	2.652	0.301
Rubus caesius	18.684	296.786	n.d.	13.734	n.d.	n.d.	n.d.	22.608	16.038	129.462	9.788	2.166
Sambucus nigra	2.995	224.568	15.712	41.876	n.d.	n.d.	n.d.	22.153	43.193	239.379	5.945	1.884
Silybum marianum	1.913	28.275	n.d.	n.d.	n.d.	n.d.	n.d.	12.195	19.913	38.080	2.214	2.732
Symphytum officinale	13.324	334.684	n.d.	215.638	n.d.	n.d.	n.d.	16.224	43.449	626.240	2.073	n.d.
Teucrium chamaedrys	3.472	80.032	n.d.	n.d.	n.d.	n.d.	n.d.	10.697	6.076	87.228	2.851	1.216
Verbascum thapsus	13.875	332.140	n.d.	n.d.	3.088	8.908	n.d.	12.630	6.576	69.142	3.609	1.878
Zingiber officinale	17.651	408.658	n.d.	34.596	4.372	5.221	n.d.	11.088	23.581	51.436	3.283	1.059

\*n.d.: not detected

magnesium) of systemically used herbs were higher than locally used herbs, but the difference also was not statistically significant ( $p>0.05$ ).

As a general perspective; fluoride, chloride, sodium, potassium, calcium and ammonium were accepted as vasoconstrictor while lithium, nitrite, nitrate and magnesium were considered as vasodilator (Bullivant *et al.* 1989; Chodobski *et al.* 1986; Dehpour *et al.* 2000; Dietz *et al.* 1984; Dietz *et al.* 1981; Fouda *et al.* 1991; H.P.Rang *et al.* 2007; Haussinger *et al.* 1983; Jeon *et al.* 2006; Kanno *et al.* 1992; Martin 2001; Rahimzadeh-Rofouyi *et al.* 2007; Singirik *et al.* 1989; Sparicio *et al.* 2004). The effects of other ions we analyzed (phosphate and sulfate) on vessels were not exactly determined. When we consider the results in respect of their effects on the vessels; it was shown that the concentration of vasoconstrictor effective ions was ( $88.60 \pm 144.27\text{mg}/100\text{g}$ ), higher than the concentration of vasodilator effective ions ( $11.99 \pm 57.39\text{mg}/100\text{g}$ ) ( $p<0.001$ ).

Also there was difference between vasodilator and vasoconstrictor ion concentrations of locally and

systemically used herbs. While vasoconstrictor ion concentration of systemically used herbs was  $88.06 \pm 147.42\text{mg}$  (mean  $\pm$  SD), vasodilator ion concentration of locally used herbs was  $90.15 \pm 136.94\text{mg}$  (mean  $\pm$  SD). The difference between vasodilator concentrations of groups was more evident;  $5.39 \pm 9.80\text{ mg}$  and  $14.32 \pm 66.48\text{ mg}$  for locally and systemically used herbs respectively.

## DISCUSSION

This study showed that herbal remedies used for the treatment of hemorrhoid in Turkey contain vasoactive and especially vasoconstrictor ions. Also some drugs with vasoconstrictor effect are used in modern medicine in order to reduce swelling and relieve itching and discomfort by tightening blood vessels (Hodes 1996; Sause 1995).

Serum electrolyte levels are strictly controlled by various homeostatic mechanisms. Therefore, ingestion of herbals for the treatment of hemorrhoids could not cause vasoconstriction in hemorrhoidal veins via their effects on blood electrolyte levels. For example, potassium could cause vasoconstriction *in vitro* above the 30 mM

concentration in human arteries and veins which is impossible to reach this level in *in vivo* conditions since potassium is strictly controlled in the range of 3.5-5.5 mEq/L (Gul *et al.* 2003; Yildiz *et al.* 2003). In adults, each 20 mEq of potassium results in average increase in serum potassium level of 0.25 mEq/L. Serum potassium level above the 5.5 mEq/L is called as a hyperkalemia and it is associated with cardiac abnormalities before its vasoconstrictor level (30 mEq/L). Namely, ingested anions or cations in herbals could not cause vasoconstriction and/or vasodilatation via their anion and cation contents since the existence of strict internal homeostasis. But, anion and/or cation levels in externally applied herbals could reach enough concentration to cause vasoconstriction in hemorrhoidal veins. As the mentioned above, vasoconstrictor ion levels of externally applied herbals is greater than their vasodilator ion contents. On the other hand, vasoconstrictor agents could amplify each others' effects as it has been previously shown, therefore it is probable that the vasoconstrictor ion contents could contribute to the curative effects of herbals in the treatment of hemorrhoids (Gul *et al.* 2002).

Also it should be noticed that other properties and constituents of these herbs may be effective in the treatment of hemorrhoids, and this may be aim of a further study.

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