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About High Potent Efficacy of FLEBIL in Pharmacotherapy of Hemorrhoidal Disease Associated with Irritable Bowel Syndrome (IBS)

Lali Dateshidze*

Department of Human Resources, Aversi Pharma, Kazbegi Street 16, Tbilisi, Georgia

*Corresponding author: Lali Dateshidze, Department of Human Resources, Aversi Pharma, Kazbegi Street 16, Tbilisi, Georgia, Tel: +995 577 27 27 46; E-mail: lali.dateshidze@aversi.ge

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Commentary

Hemorrhoid is a widely common condition, significantly worsening quality of human life. Prevalence of hemorrhoid disease ranges 44-86%. The reason of specific variability is related to society’s embarrassing attitude to the problem, a major part of patients delay a visit for medical service unless complicated condition. On the other hand, the illness nearly in 40% occurs without significant signs and symptoms.

The disease prevalence is equal in both genders and mostly frequent in ages 45-65 years. Considered, that hemorrhoid prevalence is positively correlated with social-economic state. According to WHO dates, hemorrhoid problem is common for 80% population of megalopolises.

Despite of multi-factorial basis of hemorrhoid, there is a certain facilitating or aggravating condition in this point of view. No rarely, hemorrhoid is accompanying with IBS and on the other hand, IBS can promote hemorrhoid. Presumably, there is an inter-relational link between them. Concerning IBS, it is common functional disorder of GI tract. These problems both have common attitude by a major part of patients – avoiding timely address for medical care. But ignorance of the problems can lead aggravation of the condition. There is unconfirmed consideration, that advanced case of IBS might be precondition for Crohn’s and Inflammatory Bowel Disease [1,2].

As shown in **Table 1**, like hemorrhoidal disease, the reasons of IBS are multifactorial. But unlike hemorrhoidal disease IBS diagnostics is more difficult problem because of its various signs and symptoms. It is possible each IBS patient symptoms may be completely different from one another’s. Diagnostic problem becomes complicated because there are no internal pathological changes as well. There is presented only manifested functional complex of changes without any organic harm of GI tract. The most gastrointestinal symptoms of IBS are: abdominal discomfort, abdomen cramps, motoric disorder, mucous in feces (**Table 2**). By the last sign, the disease for long time was called as mucous colitis. But point of view its physical and mental originating now is named as IBS.

Table 1 The emphasizing basis for interlink between hemorrhoid and IBS is tight mutual dependence of their reasons and symptoms. As a reason of hemorrhoid can be IBS, on the other hand hemorrhoid might be a provoking factor of IBS.

| Reasons of hemorrhoid | Reasons of IBS |
|-----------------------------------------------------|-------------------------------------|
| Irregular bowel activity (constipation or diarrhea) | Anus-rectal disorders - hemorrhoid |
| Hypodynamia | Gastroenteritis |
| Imbalanced diet | Infection diseases |
| Intra-abdominal press | Disbiosis |
| Chronic coughing | Hormonal disorders |
| Pelvis diaphragm disfunction | Gynecological |
| Hereditary predisposition | Chronic fatigue and stress |
| Age and etc. | Medications: antibacterial and ets. |
| | Hereditary predisposition |
| | Imbalanced diet |

Stress is particularly significant non-gastrointestinal symptom of IBS and moreover it is provocative factor for IBS. Consequently IBS is considered as a bio-psycho-social problem. That means that psychosocial factors lead bowel functional disorder and on the other hand, IBS problems evokes stress without any exogenous stress irritants. So it is no simple coincidence that there is high prevalence of IBS among emotional, disposed to stress individuals. Especially, vulnerable are psychic and physical violence victims. Thus is a case of revealing psychological stress by physical symptoms. In relation to IBS treatment it is significant finding recently studied IBS pathophysiology. According to this study stress-induced IBS is linked with bowel epithelium permeability changing and bowel mast cells stabilization can be the potent target for therapy of IBS [3].

On the other hand, as mast cells degranulation is the source of various vasoactive and proinflammatory substances activity, there are important issue to study new generation of mast cells stabilizers. It has been identified potent mast cells

stabilizer effect of natural components (flavonoids, phenols, terpenoids, coumarins) [4,5].

Table 2 Considerable non-gastrointestinal symptoms are typical for IBS.

| Gastrointestinal signs and symptoms | Non-gastrointestinal signs and symptoms |
|----------------------------------------------|-----------------------------------------|
| Abdominal discomfort | Insomnia |
| Abdomen cramps | Syndrome of chronic fatigue |
| Diarrhea or constipation or both alternately | Depression, chronic stress |
| Feeling of bowel incomplete emptying | Migraine-like pain |
| Meteorism | Frequent diuresis |
| Mucous feces | Chronic backache |
| | Temporomandibular joint disorder |
| | Unreasonable tachycardia |
| | Somatoform disorders |

Furthermore considerable non-gastrointestinal symptoms are typical for IBS as well. Particularly, flavonoids express mast

cells stabilizer effect, exactly among them are quercetin, rutin, fisetin, kaempferol. Furthermore quercetin decreases IL-1b, IL-6, IL-8 and TNF production and more effectively inhibits cytokines release from human mast cells, than mast cells well known stabilizer cromolyn [4-7].

The above considered all issues can be integrated to lead consequent therapeutic finding. The reasonable following arguments can be served for this.

1. Herbal composition manufactured by Aversi Racional - medication Flebil, containing sum of flavonoids, phenols, terpanoids, coumarins; components – kaempferol, quercetin, rutin, luteolin; all together defining its pharmacological effects. Actually Flebil contains dry extracts of **Table 3**:

- *Cissus quadrangularis* extract - 100 mg,
- *Aesculus hippocastanum* extract - 50 mg,
- *Vitis vinifera* extract - 50 mg,
- *Matricaria recutita* extract – 25 mg,
- *Calendula officinalis* extract -15 mg.

As a vasotropic medication Flebil increases vascular tonus, lymph drainage and capillary resistance. Thus, Flebil is indicated for the pharmacotherapy of hemorrhoid, veins varicosis and chronic venous deficiency.

Table 3 Chemical compounds and their pharmacological effects [8-10].

| Components | Botanical family | Chemical compounds | Pharmacological effects |
|-------------------------------|------------------|--------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|
| <i>Cissus Quadrangularis</i> | Vitaceae | Triterpens, beta-cyosterol, ketosteroids, phenols, tanins, carotins, vitamin C, flavonoids – quercetin and kaempferol, phytosterols; Calcium and phosphor ions. | Anti-asthenic, anti-inflammatory, analgesic, glucocorticoids antagonists' similar effect; bone and conjunctive tissues' solidating effect [7] |
| <i>Aesculus hippocastanum</i> | Hippocastanaceae | Olean type saponins, flavonoids – quercetin, kaempferol, rutin, glycoside – aescin, karotinoids, Vitamins B,K, P, polysaccharides | Capillar protective activity, improving microcirculation, anti-platelet aggregatin, venotonic, anti-inflammatory effects. |
| <i>Vitis vinifera</i> | Vitaceae | Phenol compounds, proanthocyanidins | Potent antioxydative (50-times exceeds antioxydative efficacy of vitamin E and 20-times anti-oxydative efficacy of vitamin C) anti-carcenogenic, antimicrobial, anti-inflammatory, decreases risk of cardiovascular disease, vessels varicosis and formation of atherosclerosis plaque. Normalizes capillary structure and permeability. |
| <i>Calendula officinalis</i> | Asteraceae | Terpenoids, flavonoids, coumarins, quinons, essential oils, carotinoids and amino acids. | Anti-HIV, anti-tumor, anti-inflammatory, hepato-protective spasmolytic, antiseptic, anticongestive. |
| <i>Matricaria chamomilla</i> | Asteraceae | Essencial oils, main ingredialts - α -bisabolol, α -bisabolols' oxydesA, B, and C, chamazulen and flavonoids, matricin (in extraction process is converted to chamazulen) extra, Apigenin flavonoids –small amounts of luteolin and quercetin. | Bactericidal, fungicidal, spasmolytic, anti-inflammatory, analgesic, antiseptic, antipyretic, anti-anaphylaxis, sedative, antioxydative, antidepressant, antihistaminic, diaphoretic. |

1. It is significant, that IBS pathophysiological mechanism considers mast cells stabilization as a therapeutic target for inhibition of bowel barrier disfunction [3]. On the other hand Flebil components reveal mast cells stabilization effects. Therefore it is logical to expect Flebil's potent efficacy in the pharmacotherapy of hemorrhoidal disease associated with IBS.

2. The above expressed consideration is strengthened by multilateral coincidence Flebil's components pharmacological effects with guidelines recommended for IBS treatment [6] (**Table 4**).

Table 4 Flebil's components pharmacological effects with guidelines recommended for IBS treatment [11-13].

| Recommended pharmacotherapy by guidelines | Flebil's components effects |
|--------------------------------------------|-----------------------------|
| Spasmolytics- Dicyclomine or Hyoscyanamide | spasmolytic |
| Analgesics (Acetaminophen) | analgesic |
| Laxatives | anti-inflammatory |
| Anti-Diarrheal | tonic |
| Adsorbents | antidepressant |
| Ferments | sedative |
| Probiotics | anti-oxidative |
| Tricyclic Antidepressants | antiseptic |
| Gastro Intestinal Antiseptics | |

There are marketed several medicines containing bioflavonoids, widely used for hemorrhoid treatment as they have effective anti-inflammatory and restoring normal vein function characteristics. Therefore active substances like Diosmin, Hesperidin and etc. are indicated for chronic venous insufficiency of the lower limbs, as well as hemorrhoid disease. But in doses recommended for hemorrhoid treatment, flavonoids can be a reason of gastrointestinal disturbances, headache, and especially vulnerably regarding these adverse effects are patients with IBS. Thus, administration of individually bioflavonoid-containing pills for medical treatment of hemorrhoid associated with IBS can be considered as a risk-factor of worsening IBS symptoms [13-17].

Flebil's flavonoids are combined with other natural components being effective for IBS signs and symptoms, compensating flavonoids side effects on GIT. Thus, Flebil can be considered as the preferential in the pharmacotherapy of hemorrhoid disease associated with IBS [18].

In case of clinical confirmation of the presented consideration one medication Flebil will provide effective treatment of both conditions simultaneously -hemorrhoidal disease associated with IBS, moreover it is expected other substantial results -avoiding risk of polypharmacy and reducing therapy cost.

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