Sisymbrium “Singers’ Plant” Efficacy in Reducing Perceived Vocal Tract Disability

Abstract

Sisymbrium officinale is a plant used since Greeks Medicine in vocal tract diseases to reduce disability derived from dryness, sore throat, cough,... Modern Phytopharmacology is standardizing active principles in this plant, but still few works in literature describe results known in traditional medicine.

A small group of patients treated with Sisymbrium at recommended doses described the perceived physical disability pre and post treatment by VHI (Voice Handicap Index) scores. Analysis of the difference (delta) between VHI scores seems to prove Sisymbrium efficacy in reducing perceived disability, so facilitating voice use. In this way Sisymbrium results a choice to solve patients’ discomfort, reserving “classical” treatments - NSAIDs and antibiotics - to major pathologies.

Keywords: Vocal tract; Erysimum; Sisymbrium officinale; VHI; Phytotherapy

Introduction

Sisymbrium is an annual plant, spread mostly in the Eurasiatic Region and North Africa. It is very common in bare ground, on roadsides, dumps and edges of fields. Now is a weed plant in North America, too. There are many types of Sisymbrium: the most used in vocal tract diseases is Sisymbrium officinale (L.) Scop. (Brassicaceae).

Sisymbrium in medical history

The huge amount of popular nouns given to it (Table 1) reflects the described effects of this plant on vocal tract and other “catharral” diseases: indeed this millennial belief has but a few correlations in scientific literature.

Table 1: Sisymbrium Names.

<table>
<thead>
<tr>
<th>Botanical Name</th>
<th>Sisymbrium *Officinale (L.) Scop. (*from an old Greek term for Cress)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Botanical Synonym</td>
<td>Erysimum officinale (L.)</td>
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<tr>
<td>Pharmaceutical Name</td>
<td>Herba/Semen Sisymbrii (= Herba/Semen Erysimi)</td>
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<tr>
<td>Greek</td>
<td>Ἐρύσιμον: I save sing</td>
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<tr>
<td>Latin</td>
<td>Erysimum</td>
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<tr>
<td>Italian</td>
<td>Erba cornacchia comune</td>
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<td></td>
<td>Erba dei cantanti</td>
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<td></td>
<td>Irione</td>
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<td></td>
<td>Erba crociona</td>
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<tr>
<td>English</td>
<td>Hedge mustard</td>
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<td></td>
<td>Bank cress</td>
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<tr>
<td>French</td>
<td>Herbe aux chantre</td>
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<td></td>
<td>Velar officinale</td>
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<td></td>
<td>Tortelle</td>
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<td>German</td>
<td>Rauken-Senfkraut</td>
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<td></td>
<td>Sangerkraut</td>
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<td></td>
<td>Weg-Rauke</td>
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<td>Wilder Hanf</td>
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<td>Wegesenf</td>
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<td></td>
<td>Kreuzkraut</td>
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<tr>
<td>Spanish</td>
<td>Allaria</td>
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<td></td>
<td>Hierba de los cantores</td>
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<td></td>
<td>Hierba de San Alberto</td>
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<td>Jaramago</td>
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<td>Portuguese</td>
<td>Rinchao</td>
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<td>Swedish</td>
<td>Vagsenap</td>
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<td>Chinese</td>
<td>Ting-li</td>
</tr>
</tbody>
</table>

Dioscoride recommended it in “catharralis” diseases, so also in jaundice and in poisoning. In the XVII century, Jacques Dalechamps,
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They found flavonoids, adenine, ashy [7].

8.9% to 10.2% total itols, 0.50% to 0.56% flavonoids and 9.2%
aproximately 65% is isopropyl glucosinolate, - 10.9% to 13.5% mucilages,
ae expressed as sinigrin (C10H16KNO9S2; Mr397,5) and up to

main active compounds

Main active compounds

The chemical markers of Sisymbrium officinale are sulphated compounds, particularly glucosinolates, isothiocyanates and sulphated lactones, also found in mustard oil [4]; the main glucosinolate is glucoputranjivine [5]. Historically, the sulphated compounds are reputed to stimulate the mucosal secretion in the upper respiratory tract, so increasing expectoration [6].

Dried flowering aerial parts of Sisymbrium officinale (L.) Scopoli (= Erysimum officinale L.) contain respectively 3.6.63% to 0.94% glucosinolates - where a minimum of 0.3% of total glucosinolates is expressed as sinigrin (C10H16KNO9S2; Mr397,5) and up to a 65% is isopropyl glucosinolate, - 10.9% to 13.5% mucilages, 8.9% to 10.2% total itols, 0.50% to 0.56% flavonoids and 9.2% as ash [7].

Market available preparations

The Community herbal monograph refers only to two herbal preparations 4 from Sisymbri officinialis herba: flos comminuted herbal substance and dry extract - extraction solvent ethanol 50% (V/V - volume to volume-) or water. The herbal substance is also available in combination products with other herbal or chemical substances, mainly codeine or sulfoguaajol and other herbal substances [12].

Indications

The pharmacological activity of Sisymbrium shows anti-inflamatory, analgesic, antitussive, myorelaxant and broad spectrum antimicrobial properties [13].

Politi et al. [7] Analyzed anti-inflammatory activity of Sisymbrium officinale. They found flavonoids, adenosine, adenosin, guanine and oligosaccharides. They tested topical anti-inflammatory activity in the murine Croton oil-induced ear edema model but only a modest effect was observed at high concentrations.

Eccles hypothesized a generic “placebo-like” relaxing effect from sweet gustatory perception; gustatory afferences are mediated by cranial nerves VII, IX and X (vagus nerve) and gustatory fibers are localized in the rostral part of nucleus of solitary tract (NTS), so cough center is partially overlapped by gustatory afferences and sweet taste releases opioid peptides in NTS inhibit cough stimuli. But this effect should derive from sweeteners added to erysimum, which is a bitter plant.

European Medicines Agency (EMA) monograph “Assessment report on Sisymbrium Officinale (L) Scop. herba” states that “Sisymbri officinialis herba has been in medicinal use for a period of at least 30 years as requested by Directive 2004/24/EC (European Community), thus the requirement for the qualification as a traditional herbal medicinal product is fulfilled (long-standing use) in the following indication: traditional herbal medicinal product for the relief of throat irritation such as hoarseness and dry cough. Since clinical studies with products...
containing hedge mustard have not been found in the literature well-established use cannot be recommended. The mitigating effect of the herbal substance on the pharyngeal irritation might be due to the high mucilage’s content (10.9%-13.5%) [5]. The benefit-risk balance can be considered positive. In the past, several combination products were on the market in Spain which included Erysimum Flos combined with Liquiritiae radix, Althaeae radix, Marrubii herba, Anisi fructus and/or Thymi herba. For example in Euphon® syrup and pastille until 2004 in Belgium.

**Products on the market in the EMA member states**

Regulatory status overview: Marketing Authorisation only in Belgium and Portugal while Traditional Use Registration only in Germany and France. On the counter product in other countries.

**Side effects - contraindications**

As far as now, there are no known or proved side effects for Sisymbrium. The reported pharmacological effects are not considered contradictory to the traditional uses. Specific data on pharmacokinetics and interactions are not available.

EMA in 2013 specified “Non-clinical information on the safety of *Sisymbrium officinale* could not be retrieved. However, during the long-standing use in the Member States, no adverse effects or incidences were reported.” Based on this it is concluded that there are no safety concerns relating to the use of the preparations in the given indication at the traditionally used doses.

2014 EMA monograph generally indicates contraindication in traditional use “in case of hypersensitivity to the active substance” (from the package leaflet of a Belgian product). About special warnings and precautions for use, recommend to avoid oromucosal use under 6 yrs “because of the pharmaceutical form (solid dosage form) - from the package leaflet of a French product - and due to lack of adequate data”.[(Wolf 1992)](https://www.ncbi.nlm.nih.gov/pubmed/25426518) The package leaflet of a German product shows “The use in children under 5 years of age is not recommended due to lack of adequate data.” The package leaflet Belgian product says “Spray should not be used by children under 3 years of age and oral use under 3 yrs, due to lack of adequate data and because medical advice should be sought.”

No fertility data available nor about genotoxicity. Safety during pregnancy and lactation has not been established, even if the package leaflet of a Belgian product says “The use of the syrup is not contraindicated during pregnancy and lactation,” while in the package leaflet of a German product is written “In the absence of sufficient data, the use during pregnancy and lactation is not recommended.”

No studies on the effect on the ability to drive and use machines have been performed. No undesirable effects known.

About pharmaceutical particulars, the content of cardenolides has to be specified in the herbal preparations and should be ≤1ppm. No case of overdose has been reported, even if information from the package leaflet of a German product: “Queasiness, vomiting, diarrhoea, headache and cardiac rhythm disorders have been reported.” It is conceivable that over dosage would have digitalis-like effects. These should include queasiness, vomiting, diarrhoea, headache and cardiac rhythm disorders [14], PDR for Herbal Medicines [4]. Cases of poisonings, however, have not been recorded.

About pharmaceutical interactions, the package leaflet of a German product says “Potassium deficiency. Intake of cardiac glycosides”. EMA report comments: This is only a theoretical assumption; no report is mentioned in the market overview. So no data available about pharmaceutical interactions.

**Ema’s overall conclusions on *sisymbrium officinale*’s clinical safety (2014)**

a) The medicinal use of hedge mustard preparation is considered safe because no adverse effects have been reported during the long-standing use as a medicinal product in Belgium and Germany.

b) The known toxic cardioactive steroid glycosides have been documented as a minor component and their concentrations are too low to present any risk to human health.

c) The oromucosal use in children under 6 years of age is not recommended because of the solid dosage form and due to lack of adequate data.

d) The oral use in children under 3 years of age is not recommended due to lack of adequate data and because, for the proposed indication, medical advice should be sought for this age group.

e) Since there are insufficient data, the use during pregnancy and lactation is not recommended.

**Aim of the Study**

The vocal tract needs a high level of hydration to work properly, mostly at vocal folds edges level. The risk for friction and its derived lesions is directly related to relative humidity, amount of dusts, reduction of mucus lubrication from tissues hyperemia in case of flogosys.

The aim of this work is to observe perceived vocal tract disability and its variation after a short treatment with *Sisymbrium officinale*. As to World Health Organization, the consequences of a disease may be classified as impairment, disability and handicap. Disability is described as “a restriction or lack of ability manifested in the performance of daily tasks.” Handicap is defined as, “a social, economic, or environmental disadvantage resulting from an impairment or disability.”

A widespread used method to assess perceived Voice Handicap is Vocal Handicap Index questionnaire (VHI) by Jacobson et al. [15], where handicap is measured through three different scales measuring Physical, Functional and Emotional perceived disabilities. Perception of dryness and sore throat in the vocal tract is physically disabling. The scores delta, between pre and post treatment, in Physical Scale of VHI has been chosen to describe the perceived reduction in vocal tract disability.

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Materials and Methods

Only France and Germany have products registered for traditional use [16]. In this work the Authors used French product Sisymbrium. In random serie, patients claiming vocal tract discomfort were treated with Sisymbrium, 90 mg extract/day for 10-20 days, [16] alone or with treatment related to the diagnosed disease [17].

Diagnosis was described as: Functional Dysphonia (FD), Organic Dysphonia (OD), Laryngo Pharyngeal Reflux (LPR), Upper Airways Acute Flogosis (UAAF) or Upper Airways Chronic Flogosis (UACF), obtained through ENT objective evaluations. We tried to plan a “placebo control group”, but the pharmaceutical firm did not accept to prepare it.

Patients filled a VHI - P scale before and after treatment

The patients were 64 F and 40 M, aged 8-80 yrs -mean age 42,1yrs. They were 65 artists (A), 30 non artists (NA) and 9 Voice Professionals in spoken non artistic voice (VP). 3 of them did not submit to controls (NA) so the studied group was of 62 F, 39 M; 63 A, 30 NA 8 VP. Their diagnosis distributed as 20 FD, 21 OD, 5 LPR, 14 LPR + OD, 32 UAAF 13 UACF.

Results

i. The mean VHI-P pretreatment score was 27, 9 /40: pretty high level of perceived disability. The mean VHI-P post treatment score was 13, 2: a very low level of residual disability.

ii. The average DELTA VHI was around 14/40: this means the reduction of one third of the perceived disability in a short time.

iii. In FD the treatment with Sisymbrium obtained a mean reduction of disability of 13/40.

iv. In OD the result was 13, 6/40 in Sisymbrium alone treatment, while in 10 days complex treatment the reduction was 13/40 and in 20 days 14, 4/40.

v. In LPR the treatment with added Sisymbrium gave a mean reduction of 12/40 in a 10 days treatment and 13, 9/40 in a 20 days treatment.

vi. In UAAF treated with Sisymbrium the mean perceived reduction was 15/40, 14, 9/40 in 10 days combined and 15, 6/40 in 20 days combined.

vii. In UACF treated with Sisymbrium plus FANS for 20 days, the referred reduction of perceived disability was 13, 2/40 avg.

Discussion

Politi et al. [7] evaluated Sisymbrium anti-inflammatory effects in terms of edema reduction in mice ears (inners faces of auricular pavillon) measured as weight reduction of treated samples meaning edema’s reduction. This choice might have been a limit, first because vocal tract tissues are at least of three different kinds (pseudostratified columnar, nonkeratinized and keratinized stratified squamous epithelium) while mice ear has only a stratified squamous type, and second because Sisymbrium effect does not look similar to NSAIDs, like salicylates [18-20].

In our work the main claim is physical disabling effect of dryness, related to hyperemia and sticky secretions. The effect of Sisymbrium seems mostly “moisture enhancing”, - and in this case tissues’ weights should not change that much, or better increase than decrease.

The scores show a homogenous reduction around 30% (13/40) of perceived disability. The scores seem independent from different diagnosis or single or combined treatment. So the presence of Sysimbrium in the treatment seems the common factor facilitating reduction of perceived disability.

Conclusion

Vocal tract pathologies must be treated following Evidence Based Medicine protocols. But Biagi [13] pointed out that in some cases Phytoterapy maintains a pivotal role in the modern EBM. “Main peculiar features of medicinal plants may be compared to monomolecular drugs:

a. Pharmaco-toxicological profile

b. Multitarget mechanism of action

c. Synergistic mechanism of phytocomplex”

In our work a small group of patients with different diseases of the vocal tract, all resulting in perceived physical disability, a short treatment with Sisymbrium Officinalis, alone or combined with EBM drugs, resulted efficient in reducing disability. This observation seems coherent to traditional medicine expectations [21,22].

So we can conclude that, in diagnosed absence of major diseases, when in a Patient the desired effect is simply prompt reduction of perceived disability to reduce resulting handicap, if prescribed under physician control and instrumental assessment, monitoring subjective perception of symptoms, phytotherapy may show efficacy and cost/effectiveness, where “main classical treatments” may be expensive, redundant or present undesired side effects.

References

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