



EUROPEAN MEDICINES AGENCY  
SCIENCE MEDICINES HEALTH

20 November 2018  
EMA/HMPC/638127/2019  
Committee on Herbal Medicinal Products (HMPC)

## Overview of comments received on draft *Fragaria vesca* L.; *Fragaria moschata* Weston; *Fragaria viridis* Weston; *Fragaria x ananassa* (Weston) Duchesne ex Rozier, folium

Table 1: Organisations and/or individuals that commented on the draft European Union herbal monographon *Fragaria vesca* L.; *Fragaria moschata* Weston; *Fragaria viridis* Weston; *Fragaria x ananassa* (Weston) Duchesne ex Rozier, folium as released for public consultation on 15 April 2018 until 15 July 2018.

	Organisations and/or individuals
1	EURORDIS (Rob Camp)
2	European Public Health Alliance (Joseph Shafer)

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Table 2: Comments

### Specific comments on text

Section number and heading	Interested party	Comment and Rationale	Outcome
1	R. Camp (Eurordis)	Dysuria – 4/5 people in my office didn't know what it is.	<p>Not endorsed.</p> <p>Dysuria is a symptom of pain, discomfort, or burning when urinating. One of the main causes of painful urination are urinary tract infections.</p> <p>The term dysuria is a standard term and is used in all EMA monographs of diuretics.</p>
2	J. Shafer (EPHA)	General commentary: There are some who believe that the <i>F. ananassa</i> (garden variety) has less effect than that of the <i>vesca</i> (wild). The conclusion is still out, but it might be something of import to note. Below is a medicinal rating chart for the various forms. <i>FV</i> shows the highest level with <i>moschata</i> , <i>viridis</i> and <i>ananassa</i> all rated 0.	<p>Not endorsed.</p> <p>Herbal preparations covered by this AR and MO should comply with the official quality reference: a monograph exists at the Austrian Ph (Österreichisches Arzneibuch 2013, DAC 2004), where <i>Fragaria</i> leaves are defined as "The collected, dried leaves of <i>Fragaria vesca</i> L., <i>Fragaria moschata</i> Weston, <i>Fragaria viridis</i> Weston, <i>Fragaria x ananassa</i> (Weston) Duchesne ex Rozier or a mixture of these species. Content: at least 3% of tannins expressed as pyrogallol (C<sub>6</sub>H<sub>6</sub>O<sub>3</sub>; Mr 126.1) and based on the dried drug.</p> <p>The cited sentence: "the wild form was characterized by higher levels of examined substances" from the publication:</p> <p>Najda <i>et al.</i> Ann Agric Environ Med 2014; 21(2):339–</p>

Section number and heading	Interested party	Comment and Rationale	Outcome																																																								
		<table border="1"> <thead> <tr> <th>Latin Name</th><th>Common Name</th><th>Edibility Rating</th><th>Medicinal Rating</th></tr> </thead> <tbody> <tr> <td><i>Fragaria</i></td><td>Strawberry, Beach strawberry, Pacific beach strawberry, Sandwich beach strawberry, Virginia strawber</td><td>3</td><td>0</td></tr> <tr> <td><i>Fragaria bracteata</i></td><td>Woodland Strawberry</td><td>2</td><td>0</td></tr> <tr> <td><i>Fragaria californica</i></td><td>Californian Strawberry</td><td>2</td><td>1</td></tr> <tr> <td><i>Fragaria chiloensis</i></td><td>Beach Strawberry, Pacific beach strawberry, Sandwich beach strawberry</td><td>2</td><td>1</td></tr> <tr> <td><i>Fragaria daltoniana</i></td><td></td><td>2</td><td>1</td></tr> <tr> <td><i>Fragaria inumae</i></td><td>Strawberry</td><td>2</td><td>0</td></tr> <tr> <td><i>Fragaria moschata</i></td><td>Hautbois Strawberry</td><td>3</td><td>0</td></tr> <tr> <td><i>Fragaria nilgerrensis</i></td><td></td><td>2</td><td>0</td></tr> <tr> <td><i>Fragaria nipponica</i></td><td></td><td>2</td><td>0</td></tr> <tr> <td><i>Fragaria nubicola</i></td><td>Indian Strawberry</td><td>2</td><td>1</td></tr> <tr> <td><i>Fragaria orientalis</i></td><td></td><td>3</td><td>0</td></tr> <tr> <td><i>Fragaria ovalis</i></td><td>Rocky Mountain Strawberry</td><td>3</td><td>0</td></tr> <tr> <td><i>Fragaria vesca</i> 'Semperflorens'</td><td>Alpine Strawberry</td><td>5</td><td>3</td></tr> </tbody> </table> <p>Comparative analysis of secondary metabolites contents in <i>Fragaria vesca</i> L. fruits</p> <p>Ann Agric Environ Med 2014; 21(2):339–343 “the wild form was characterized by higher levels of examined substances”</p>	Latin Name	Common Name	Edibility Rating	Medicinal Rating	<i>Fragaria</i>	Strawberry, Beach strawberry, Pacific beach strawberry, Sandwich beach strawberry, Virginia strawber	3	0	<i>Fragaria bracteata</i>	Woodland Strawberry	2	0	<i>Fragaria californica</i>	Californian Strawberry	2	1	<i>Fragaria chiloensis</i>	Beach Strawberry, Pacific beach strawberry, Sandwich beach strawberry	2	1	<i>Fragaria daltoniana</i>		2	1	<i>Fragaria inumae</i>	Strawberry	2	0	<i>Fragaria moschata</i>	Hautbois Strawberry	3	0	<i>Fragaria nilgerrensis</i>		2	0	<i>Fragaria nipponica</i>		2	0	<i>Fragaria nubicola</i>	Indian Strawberry	2	1	<i>Fragaria orientalis</i>		3	0	<i>Fragaria ovalis</i>	Rocky Mountain Strawberry	3	0	<i>Fragaria vesca</i> 'Semperflorens'	Alpine Strawberry	5	3	343 refer to the results of comparative studies of the content of active substances in the fruits, not in the leaves of <i>Fragaria vesca</i> , which is the subject of the monograph.
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4		<p>The section on uses is based on well-established/traditional use, but the notations seem a bit tepid to say the least. There is a diuretic effect that is traditional as well as gastrointestinal,</p>	<p>Not endorsed.</p> <p>We do not have reliable data confirming any clinical studies of <i>Fragaria vesca</i> leaves. Nor is any medicinal</p>																																																								

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		<p>not just diarrhoea. FV leaf tea was also used for GI distress, not just mild diarrhoea as is noted in the monograph.</p> <p>It has been used for chilblains and externally for sunburn.</p> <p>An oil-based poultice was used for open sores.</p> <p>King's American Dispensatory of 1898 -The leaves are astringent with diuretic and diaphoretic properties.</p>	<p>product authorised for medicinal use in the EU to fulfil provisions of Art. 10a Directive 2001/83/EC (well-established use).</p> <p>Thus, the indications in the monograph are based on &gt; 30 years European traditional usage. There is insufficient information from American sources about traditional use, even valuable and old ones, that would provide additional information regarding specified use, strength and posology according to requirements of Chapter 2a of Directive 2001/83/EC (traditional use).</p>
4		<p>There is also a growing amount of research into FV leaf that has not been mentioned that notes the anti-oxidant properties of the plant:</p> <p>Combination of LC-MS based metabolomics and antioxidant activity for evaluation of bioactive compounds in <i>Fragaria vesca</i> leaves from Italy.</p> <p>Article: Dec 2017J PHARMACEUT BIOMED.</p>	<p>Not endorsed.</p> <p>Antioxidant activity is a general effect exerted by most herbal substances/preparations with a high polyphenols content. This effect does not support any other activity which should be assessed by specific experimental designs</p>
4		<p>Promising Health Benefits of the Strawberry: A Focus on Clinical Studies. Sadia Afrin † , Massimiliano Gasparrini † , Tamara Y. Forbes-Hernandez † ‡ , Patricia Reboredo-Rodriguez † § , Bruno Mezzetti  , Alfonso Varela-López⊥, Francesca Giampieri* † , and Maurizio Battino* † #</p>	<p>Not endorsed.</p> <p>This review publication applies only to the health benefits of fruits of <i>Fragaria</i> spp. not the leaves that are the subject of the monograph.</p>

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		J. Agric. Food Chem., 2016, 64(22), pp 4435–4449.	
4		<p>Molecular and cellular targets of polyphenols from <i>Fragaria vesca</i> leaf.</p> <p>Joana Liberal, University of Coimbra, Portugal</p> <p>J Pharma Care Health Sys</p>	<p>Not endorsed.</p> <p>Cited publication is a report at the European Pharma Congress in the form of a single-page abstract: (Molecular and cellular targets of polyphenols from <i>Fragaria vesca</i> leaf, European Pharma Congress</p> <p>Joana Liberal, University of Coimbra, Portugal</p> <p>Scientific Tracks Abstracts: J Pharma Care Health Sys DOI: 10.4172/2376-0419.S1.005).</p> <p>The results of studies presented at the Congress are included in:</p> <p>Liberal J <i>et al.</i> Bioactivity of <i>Fragaria vesca</i> leaves through inflammation, proteasome and autophagy modulation. J. Ethnopharmacol 2014; 158:113-22 and are discussed in the preclinical part of the Assessment Report and included in the Reference List.</p>