European Medicines Agency
Evaluation of Medicines for Human Use

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COMMITTEE ON HERBAL MEDICINAL PRODUCTS (HMPC)

FINAL

PUBLIC STATEMENT ON THE USE OF HERBAL MEDICINAL PRODUCTS CONTAINING ASARONE

DISCUSSION IN HMPC	January 2005 March 2005
RELEASE FOR CONSULTATION	April 2005
DEADLINE FOR COMMENTS	June 2005
REDISCUSSION IN HMPC	November 2005
ADOPTION BY HMPC	November 2005

The Committee on Herbal Medicinal Products endorses without any changes the 'Position Paper on the use of herbal medicinal products containing asarone' adopted by the Herbal Medicinal Products Working Party (HMPWP) in December 2003.

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Public Statement on the use of herbal medicinal products containing asarone

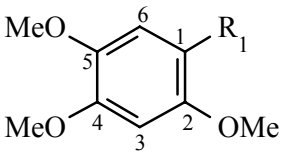
I. ASARONE

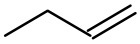
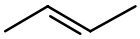
Registry Number: 494-40-6

Formula : $C_{12}H_{16}O_3$

Mw : 208,255

Synonyms : 1(2,4,5-trimethoxyphenyl)-1-propene ; asarone ; asarum camphor



R_1	
	γ-asarone
	β-asarone
	α-asarone

* α -asarone = 1,2,4-trimethoxy-5-(1-propenyl)benzene, 9CI (E) form

Registry Number : [2883-98-9]

Synonyms :
- trans- α -asarone
- isoasarone

* β -asarone = 1,2,4-trimethoxy-5-(1-propenyl-benzene, 9CI (Z) form

Registry Number : [5273-86-9]

CA Index name : Benzene, 1,2,4-trimethoxy-5(12)-1-propenyl-(9CI)

Synonyms :
- β-asarone (6CI)
- Benzene, 1,2,4-trimethoxy-5-[1-propenyl)-,(Z)-
- Benzene, 1,2,4-trimethoxy-5-propenyl-,(Z)-(8CI)
- (Z) asarone
- cis- β-asarone
- cis-asarone
- cis-isoasarone

* γ -asarone = 1,2,4-trimethoxy-5-(2-propenyl)benzene

Registry Number : [5353-15-1]

Synonyms :
- Euasaron
- Isoasaron
- Sekishon

II. β-asarone is a natural constituent of some aromatic plants and their essential oil fractions, especially of species of the genus *ACORUS* (Araceae).

EO = Essential Oil, MEOC = Major Essential Oil Component

Botanical name	**Plant part**	**Content of β-asarone**
Acorus calamus var. *americanus* (Raf.) Wulff.		
(= *Acorus americanus* Raf.) (Diploïd.)	Leaf (EO)	not detected
	Rhizome (EO)	not detected
Acorus calamus L. var. *calamus*		
(=Acorus calamus L.var. vulgaris L.)(Triploïd)	Leaf (EO)	50-65 %(MEOC)
	Rhizome(EO)	9-19 %(MEOC)
	Dried rhizome	0.3%
Acorus calamus L. var.*angustatus* Bess		
(= *Acorus triqueter* Turcz.) (Tetraploïd)	Leaf (EO)	MEOC
	Rhizome (EO)	85 - 95 %
	Dried rhizome	4.4 – 8.3%
Orthodon asaroniferum Fujita	Not identified in literature (EO)	25%
Orthodon isomyristicineferum Fujita	Not identified in literature (EO)	25 %
Piper lolot DC.	Rhizome and Root exts	38 % in n-hexan extracts

Asarone (α and β or α or β) has also been reported to occur in the following plants, but its content has not been mentioned:

Acorus gramineus Ait. (asarone*) ; *Asarum europaeum* L. (α-asarone) ; *Asarum arifolium* Michx (α-asarone); *Daucus carota* L. (α-asarone); *Helichrysum arenarium* (L.) Moench. (β-asarone); *Magnolia salicifolia* Maxim.(α-asarone); *Piper angustifolium* R. & P. (asarone*); *Piper sumatranum* DC. var. *andamanica* (asarone*); *Sassafras albidum* (Nutt.) Nees (asarone*) - * unspecified

III. Medicinal uses

The rhizomes of *A. calamus* are used extensively in traditional medicine worldwide.

Reported uses include: stomach cramps;
dysentry;
asthma;
anthelmintic;
insecticide;
tonic;
stimulant.

IV. Toxicity

Mammalian toxicity and carcinogenicity of asarones (α and β) has been demonstrated.

The alkenylbenzenes, α- and β-asarone, are genotoxic and hepatocarcinogens in rodents.

V. Pharmacology

α- and β-asarone demonstrated:

- a mobility inhibition (α and β)
- a nematocidal activity (α and β)
- anticoagulant effect in the mouse and the rat (β)
- sedative and hypothermic effects in rats (β)
- insecticidal activity (LC_{100} = 16 µg /ml) using the *Aedes aegypti* larvicidal assay (β)
- feeding-deterrent activity against some stored Coleoptera (α)

α- and β-asarone exhibit neuroprotective action against the NMDA - or Glutamic acid - induced excitotoxicity through the blockade of NMDA receptor function.

Conclusion

In view of the toxicity of α- and β-asarone, their concentration in herbal medicinal products should be reduced to minimum and diploid varieties should always be preferred.

In analogy with the food regulation (limitation of the intake of β-asarone from food and alcoholic beverages), a limit of exposure from herbal medicinal products of approximately 115 µg/day, i.e. about 2 µg/kg bw/day could be accepted temporarily until a full benefit/risk assessment has been carried out.

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