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WORKING PARTY ON HERBAL MEDICINAL PRODUCTS

**FINAL POSITION PAPER ON THE USE
OF HERBAL MEDICINAL PRODUCTS CONTAINING ASARONE**

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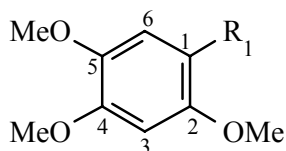
I. ASARONE

Registry Number: 494-40-6

Formula : C₁₂H₁₆O₃

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
<i>Acorus calamus</i> var. <i>americanus</i> (Raf.) Wulff. (= <i>Acorus americanus</i> Raf.) (Diploïd.)	Leaf (EO)	not detected
	Rhizome (EO)	not detected
<i>Acorus calamus</i> L. var. <i>calamus</i> (= <i>Acorus calamus</i> L. var. <i>vulgaris</i> L.) (Triploïd)	Leaf (EO)	50-65 % (MEOC)
	Rhizome (EO)	9-19 % (MEOC)
	Dried rhizome	0.3%
<i>Acorus calamus</i> L. var. <i>angustatus</i> Bess (= <i>Acorus triqueter</i> Turcz.) (Tetraploïd)	Leaf (EO)	MEOC
	Rhizome (EO)	85 - 95 %
	Dried rhizome	4.4 – 8.3%
<i>Orthodon asaroniferum</i> Fujita	Not identified in literature (EO)	25%
<i>Orthodon isomyristicineferum</i> Fujita	Not identified in literature (EO)	25 %
<i>Piper lolot</i> 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;
- dysentery;
- 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 ($LC_{100} = 16 \mu\text{g/ml}$) 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 $115 \mu\text{g/day}$, i.e. about $2 \mu\text{g/kg bw/day}$ could be accepted temporarily until a full benefit/risk assessment has been carried out.

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