Annex 5 to 5-3539-02-5543103

Scientific assessment of yohimbe (*Pausinystalia yohimbe*)

Subject of the assessment

In collaboration with the ALS working Group "Diätetische Lebensmittel, Ernährungs- und Abgrenzungsfragen", the Federal Office of Consumer Protection and Food Safety (BVL) has drafted a “hit list” of 10 substances whose consumption is detrimental to human health. These plants, which include Yohimbe (*Pausinystalia yohimbe* (K. Schum.) Pierre ex Beille), and preparations made from it, contain substances with strong pharmacological and/or psychoactive effects. The European Commission was asked by the Federal Ministry of Food, Agriculture and Consumer Protection to implement the procedure under Article 8 of Regulation (EC) No. 1925/2006 for these plants, and to include them in one of the three Annex III lists. The assessment will affect the bark of the plant, as only this is known to be used. The risk assessment was carried out on the basis of the guidelines published by the EFSA for the assessment of botanicals and botanical preparations for use in food supplements[1] and of the BfR’s guidelines on health assessments[2].

Results

There are no clinical data available on the effects of yohimbe bark and preparations made from them. Yohimbine hydrochloride (yohimbine HCl), an analogue of the main alkaloid of yohimbe bark, is the only element for which an identification and assessment of dangers can be carried out. The effect of yohimbine HCl varies widely from one individual to another. Matrix effects of the plant material when the bark or preparations from the bark are used cannot be ruled out. These effects could result in the effects of individual substances being strengthened or reduced. An assessment of the risks of yohimbe bark and preparations made from it based on the available data at level A[1] show that the use of yohimbe bark and preparations made from it may be harmful to human health, although there is still scientific uncertainty on this matter.

Opinion

1. Identity of the plant (Kuhlmann, 1999; HagerROM, 2006; Wink et al., 2008; ACS, 2009; USDA, 2009)

- Family: *Rubiaceae* (bedstraw)
- Tribe: *Naucleeae*
- Genus: *Pausinystalia* L.
- Species: *Pausinystalia yohimbe* (K. Schum.) Pierre ex Beille
- Synonyms: *Pausinystalia johimbe, Corynanthe yohimbe, Corynanthe johimbi, Corynanthe yohimbi*
- common names: Yohimbe, Johimbe, Liebesbaum, Lustholz, Potenzbaum
- Parts of the plant being assessed: Bark (Potenzrinde, Yohimbe cortex, Cortex Yohimbehe)

[1] European Food Safety Authority (2009) Guidance on Safety assessment of botanicals and botanical preparations intended for use as ingredients in food supplements. http://www.efsa.europa.eu/cs/BlobServer/Guidance_of_Panel/sc_op_ej1249_botanicals_en.pdf?ssbinary=true

[2] http://www.bfr.bund.de/cm/221/bfr_leitfaden_fuer_gesundheitliche_bewertungen.pdf

- Geographical origin: tropical West Africa (Cameroon, Congo, Gabon, Equatorial Guinea, Nigeria)
- Growing and harvesting conditions: Gathering from wild plants, as the tree cannot be cultivated.

2. Applicable manufacturing methods

Dried bank from the twigs and stalk of the yohimbe tree are used in their entirety, cut up or ground into powder to use as a drug. Yohimbe is also offered as an extract (CAS: 85117-22-2) (HagerROM, 2006). There is no information on standardisation processes in cultivation. Yohimbine, the main component, can either be obtained from the bark or chemically synthesised (HagerROM, 2006).

3. Chemical composition

Alkaloid content data vary, depending on the method used. The total alkaloid content of the bark is 2–61 mg/g, while the drug should contain ≥ 15 mg/g (Brandt, 1922; Madaus, 1938; Betz et al., 1995; HagerROM, 2006). Another source says the drug should contain from 30 to 150 mg/g monoterpene indole alkaloids of the yohimbe bark type (Wink et al., 2008). The alkaloid content increases with the age of the branches (HagerROM, 2006). A preparation made from the extract should contain 95-105 mg/g of total alkaloids, calculated as yohimbine (HagerROM, 2006).

The main alkaloid is yohimbine (Table 1). The other components are primarily yohimbine stereoisomers or derivatives thereof (Table 1) and tannins (Brandt, 1922; Duke, 1992; Tam et al., 2001; HagerROM, 2006; Giftpflanzen - Pflanzengifte, 2008; RÖMPP Online, 2009).

The yohimbine content in the bark is given as 7-115 mg/g[3] and is usually around 10 mg/g (Betz et al., 1995; Zanolari et al., 2003; HagerROM, 2006; Chen et al., 2008). The values depend largely on the method used (Zanolari et al., 2003). Yohimbine is well soluble in alcohol and poorly soluble in water (National Toxicology Program, 1999; HagerROM, 2006)

A variety of yohimbe bark extracts are offered as monopreparations or combined with other substances in liquid, powder, capsule or tablet form. The quantities of yohimbine in these products vary. A study conducted by Betz et al (1995) showed that extracts contain a maximum of 7% of the yohimbine detectable in the bark, with the majority of products having a significantly lower to zero detectable yohimbine content. The authors explain this by the very high rate of dilution of the end-product and by watery extraction methods. The latter methods are poorly suited to transferring the alkaloids, which are poorly soluble in water, to the extract. The highest content was found in liquid products with a high ethanol content (≈70%) (0.03% and 0.05% yohimbine). Another study of the yohimbine content of aphrodisiacs shows that the yohimbine concentrations did not always correspond to the quantities detected, some products having more (double) and others less (down to one-tenth) of the stated content (Zanolari et al., 2003).

4. Specification

No specifications are known.

[3] 11 mg/g with GC-MS (Chen et al., 2008); 7 mg/g with GC (Betz et al., 1995); 8, 12, 22 mg/g (HagerROM, 2006); 13 mg/g with HPLC-UV, 54 mg/g with HPLC-APCI/MS and 115 mg/g with HPLC-ESI/MS (Zanolari et al., 2003)

5. Stability of the plants and plant preparations used

Yohimbe bark
No data are available for yohimbe bark or extracts thereof.

Yohimbine
When used for medicinal purposes, yohimbine should be kept away from light (HagerROM, 2006).

6. Use and quantities suggested as a foodstuff

There is no information on its use as a food in Germany.

7. Other uses

Yohimbe bark
Yohimbe bark extract was originally used in tropical Africa as a stimulant and a tonic for men. Little is known about the frequency of use, the method of consumption, the amount consumed and length of consumption (Kuhlmann, 1999).
Nowadays it is used to treat sexual dysfunction and erectile problems (www.biovea-deutschland.com, 2009). It is either taken in the form of tea, or in capsules and tablets (NCCAM, 2009).

Yohimbine
Yohimbine, the main alkaloid, occurs in drugs in the form of yohimbine-HCl (CAS: 65-19-0) for treating erectile dysfunction and climacterium virile (Fachinformation Yohimbin "Spiegel"®, 2008). It is also given to bodybuilders as a weight-loss and performance enhancement drug (National Toxicology Program, 1999; www.body-academy.com, 2009).

8. Assessments by other organisations

Yohimbe bark
In 2007/2008, the *National Center for Complementary and Alternative Medicine* (**NCCAM**) found that it is unknown whether yohimbe/yohimbe bark can affect health in any way, as no trials have been conducted with yohimbe bark or extracts made from it (NCCAM, 2008).

Yohimbe bark and yohimbine
Because it is used as a food supplement in the USA, and because of its structural similarity to reserpine (which is carcinogenic), yohimbe bark extract and yohimbine was proposed for assessment by the **National Toxicology Program**. There is no information in the literature on the genotoxicity or carconogenicity of yohimbe or yohimbine (National Toxicology Program, 1999).

Table 1: Yohimbe bark aklaloids

Name	Synonyms	CAS
Yohimbine	17α-Hydroxyyohimban-16α-carboxylacidmethyl-ester Johimbin Quebrachine Aphrodine Corynine Corymbine Yohimvetol Hydroaerogotocine	146-48-5
α-yohimbine	Rauwolscine Corynanthidine Isoyohimbine Mesoyohimbine	131-03-3
β-yohimbine	Amsonine	549-84-8
Pseudoyohimbine		84-37-7
Corynanthine	Rauhimbine	483-10-3
Alloyohimbine		522-94-1
Ajmaline	Rauwolscine Tachmaline	4360-12-7
Ajmalicine	Raubasine d-yohimbine	483-04-5
Corynantheine		
19-Dehydroyohimbine		
Dihydrocorynantheine		
Dihydrosissirikin		
Tetrahydromethylcorynantheine		

Yohimbine

Commission E of the Bundesgesundheitsamt has assessed yohimbehe cortex (yohimbe bark consisting of dried bark from the trunk and stems of *Pausinystalia yohimbe* and preparations made from them) as a herbal medicine. Its therapeutic use to treat sexual dysfunction, as an aphrodisiac and for fatigue and exhaustion, has been rejected because of inadequate proof of its efficacy, and the inability to carry out a risk-benefit assessment. The risks in the therapeutic use of the main alkaloid yohimbine are excitation, tremor, insomnia, fear, hypertension, tachycardia, nausea and vomiting. There were also interactions with psychotropic pharmaceuticals. However, it notes that these observations have not been documented for preparations using yohimbe bark (Kommission E, 1987; Kommission E, 1990).

Yohimbinic acid and esters thereof (yohimbine) are prescription-only drugs (**AMVV**, Anlage 1)

Yohimbine and yohimbine salts are prohibited in cosmetics (Regulation (EC) No. 1223/2009, Annex II)

9. Exposure data and assessments

Yohimbe bark extract and yohimbine are marketed as food supplements. US studies even speak of “significant human exposure through use as a dietary supplement” (National Toxicology Program, 2008). Depending on the recommended daily dose, users take from 1.3 to 23.2 mg of yohimbe bark extract (Zanolari et al., 2003). There are no data available to for an exposure assessment.

10. Identification and characterisation of dangers

Yohimbe bark
Only uncorroborated individual reports are available on the effect and toxicokinetics of yohimbe bark and extracts made from it (HagerROM, 2006; NCCAM, 2008).

Yohimbine
a) Pharmacokinetic properties
In contrast to yohimbe bark and yohimbe bark extracts, numerous studies on yohimbine-HCl are available. The majority of publications, however, do not distinguish between yohimbine and yohimbine hydrochloride. This means that in this text, a distinction can only been made where precise details have been stated in the sources referred to.
Table 2 summarises the pharmacokinetic data on yohimbine-HCl in various studies. Yohimbine-HCl is rapidly absorbed (≈11 min half life) and the maximum plasma concentration is generally achieved in less than one hour (Owen et al., 1987; Tam et al., 2001). The mean bioavailability is low (22–33%) and is subject to very high variation from one individual to another, ranging from 4% to 87% (Guthrie et al., 1990; Le Verge et al., 1992; Le Corre et al., 1999). The simultaneous consumption of fat-rich food reduces the absorption of yohimbine-HCl (Grasing et al., 1996). The plasma concentration of yohimbine appears to correlate only a little with the quantity of yohimbine-HCl administered (Table 2). No concentration was observed after oral intake over 6 days (3x daily 5.4 – 21.6 mg)(Sturgill et al., 1997). The distribution volume of yohimbine is relatively low, although it is a lipophile substance. That is why Le Corre et al (1999) assume that yohimbine is a class II substance in the biopharmaceutical classification of drugs, with a low solubility and high permeability. These substances are subject to a variable absorption, depending on the matrix (Le Corre et al., 1999).

Yohimbine is generally quickly eliminated from the plasma, although here too there are broad differences from one individual to another (Table 2). Clearance generally takes place via the liver metabolism, and less than 1% is excreted in the urine (Tam et al., 2001). Yohimbine is metabolised into the active metabolites 11-hydroxy-yohimbine and the les active 10-hydroxy-yohimbine (Berlan et al., 1993; Le Corre et al., 1999; Fachinformation Yohimbin "Spiegel"®, 2008). Metabolisation into 11-hydroxy-yohimbine is subject to a broad variation range (> 1000 times) (Le Corre et al., 2004). Out of 172 persons, no plasma 11-hydroxy-yohimbine was found in 17 persons, mainly of European origin (a significant ethnic difference). In the remaining 155, 12 % of the yohimbine-HCl applied intravenously (137 µg/kg[4]) was oxidised into 11-hydroxy-yohimbine. This is achieved above all through cytochrome P450 2D6 (CYP2D6). *In vivo* the extent of the yohimbine metabolism is determined by the CYP2D6 and the CYP3A4 genotypes. Wild types of both genes correspond to an extensive metabolism. The data do not indicate whether this also applies after oral administration or whether further CYPs in the intestines and liver play the decisive role (Le Corre et al., 2004).

After oral administration the AUC values for the active metabolic product of yohimbine, 11-hydroxy-yohimbine, is approximately 45 ± 36 times (0.6–118) higher than for yohimbine. The area below the concentration-time curve of 11-hydroxy-yohimbine (39– 152 µg/min/ml) varies less than for yohimbine (0,5–106 µg/min/ml). Furthermore, 11-hydroxy-yohimbine has a longer elimination half-life (Le Verge et al., 1992; Le Corre et al., 1999). 10-hydroxy-yohimbine is inactive and only detected in the urine, but not in the plasma (Le Corre et al., 1999). It oxidises into 10-hydroxy-

[4] 70 kg → 9.59 mg yohimbine

yohimbine primarily through CYP3A4 (Le Corre et al., 2004). Of the yohimbine-HCl taken in, 0.05% ± 0.06% yohimbine, 0.3% ± 0.1% 11-hydroxy-yohimbine (more water-soluble and lower plasma protein binding than yohimbine) and 14.3% ± 2.3% of 10-hydroxy-yohimbine were excreted via the liver (Le Corre et al., 1999).

The pharmacokinetics of yohimbine HCl varies widely from one individual to another. Regular administration of yohimbine HCl (three times daily for 6 days) had no effect on the pharmacokinetics. With most individuals, the pharmacokinetics correspond to a single compartment model, but with some to a two compartment model (Sturgill et al., 1997).

Table 2: Pharmacokinetics of yohimbine HCl after single oral intake (MW – mean value, SD – standard variation). The highest and lowest values are given in brackets. Figures with ≈ have been computed (dose) or taken from a figure

Dose	n	C_{max} (ng/ml)		t_{max} (h)		$t_{1/2}$el (h)		AUC (ng*h/ml)		Clearance (l/h/kg)		Distribution volume (l/kg)		Reference
		MW	SD	MW	SD	MW	SD	MW	SD	MW	SD	MW	SD	
5.4 mg	6	20		0.4			0.5							(Grasing et al., 1996)
5.4 mg	4[e]	51	46	0.4	0.3	0.3	0.2	31	15					(Sturgill et al., 1997)
5.4 mg	2[f]	281	250	0.5	0.2	2.2	1.8	580	647					(Sturgill et al., 1997)
8 mg	11	58 (3-266)	85	1.2 (0.5-2)	0.6	1.5 (0.4-4.4)	1.3	211 (8-1760)	518					(Le Corre et al., 1999)
10 mg	7	(≈7–300)		(0.2-0.8)				134 (10.7-656)	231	3.4	3.9	3.2	3.6	(Guthrie et al., 1990)
10 mg	8					0.6	0.3			2.8	1.2	2.2	1.3	(Owen et al., 1987)
10.8 mg	6	≈130 (max. 504)		0.3		0.3		≈100 (max. 550)						(Grasing et al., 1996)
10.8 mg[g]	6	≈100			0.7		0.5	≈70						(Grasing et al., 1996)
10.8 mg	4[e]	154	107	0.5	0.1	0.2	0.1	119	73					(Sturgill et al., 1997)
10.8 mg	2[f]	502	493	0.4	0.3	3.7	0.6	2230	2920					(Sturgill et al., 1997)
0.2 mg/kg (≈11,2 mg)	6	38	15				0.6	50	42	6.3	1.5	2.7	0.5	(Berlan et al., 1991)
16.2 mg	6	≈80		0.6		0.4		≈120						(Grasing et al., 1996)
16.2 mg	4[e]	400	314	0.4	0.2	0.3	0.1	376	374					(Sturgill et al., 1997)
16.2 mg	2[f]	221	49	0.5	0.1	0.9	0.3	250	18.4					(Sturgill et al., 1997)
0.2 mg/kg[h] (≈18,8 mg)	10	168	29				0.6	244	147	1.0	0.2	1.0	0.2	(Berlan et al., 1991)
21.6 mg	6	≈150		0.6		0.5		≈220						(Grasing et al., 1996)
21.6 mg	3[e]	50	19	0.4	0.1	0.2	0.1	72	42					(Sturgill et al., 1997)
21.6 mg	3[f]	201	70	0.6	0.3	8.3	11.6	1430	1980					(Sturgill et al., 1997)

[e] single compartment model
[f] double compartment model
[g] accompanied by a fatty diet
[h] overweight people, MGI: 36.4±2.1

b) Pharmacological and toxicological properties

Yohimbine HCl (an α_2-adrenoreceptor antagonist and, less pronouncedly, an α_1-adrenoreceptor antagonist) is therapeutically used primarily to treat erectile dysfunction. Although 34–86% of patients respond to treatment, because of the pronounced placebo effects, only few studies show significant pharmacological effects compared with the control group (Tam et al., 2001). To treat loss of libido and climacterium virile, 5-10 mg of yohimbine HCl are taken, preferably during meals. The desired effect sometimes occurs with a latency period of 2-3 weeks (Fachinformation Yohimbin "Spiegel"® , 2008)

The side effects of yohimbine HCl include high blood pressure and heart rate, palpitations, insomnia, irritability, excitation, shivering, sweating, flushing and headaches. Occasionally (in 0.1–1% of cases) patients have gastrointestinal symptoms such as nausea, vomiting, lack of appetite and diarrhoea. Rarely (0.01–0.1%) there are cases of hypotonic dysregulation (Fachinformation Yohimbin, "Spiegel"®, 2008). The increased norepinephrine plasma level and its metabolite 3-Methoxy-4-hydroxyphenylglycol (MHPG) is one of the most common endocrine effects of yohimbine HCl. Depending on the yohimbine plasma level, the plasma cathecholamine concentrations can increase. These effects may be accompanied by changes in blood pressure, pulse or mood changes (paranoia) (Grasing et al., 1996; Sturgill et al., 1997). Yohimbine HCl increases heart performance, increasing cardiac output and blood pressure (Le Corre et al., 2004). Although dose-dependent, this effect varies widely from one individual to another. Tam et al (2001) summarised 22 studies in which yohimbine was orally administered and the effects on blood pressure and pulse were investigated. Concentrations of 4–16.2 mg (as a single dose or three times daily) do not generally affect the blood pressure and pulse in patients with normal blood pressure. 20–30 mg of yohimbine either have no significant effect, or result in a moderate increase in blood pressure but without affecting the heart rate. Concentrations of 45.5 mg and above occasionally increase the medium arterial blood pressure, and less commonly, the heart rate. If such haemodynamic effects occur, they reach their maximum level after 60-90 mins and fall again over a few hours. Both young and older people tolerate yohimbine well in these concentrations. The side effects of yohimbine are clearly dose-related. While in therapeutic doses small or mild side-effects occur, they accumulate in higher doses (Tam et al., 2001). Yohimbine can increase the plasma concentration of free fatty acids, although this does not necessarily result in weight loss. The time at which yohimbine is taken compared with food intake plays a role in the effect of yohimbine (Galitzky et al., 1988; Berlan et al., 1991).

In case of overdose, weakness, generalised paraesthesia, loss of coordination and memory problems, as well as severe headaches combined with dizziness, tremor, palpitations and fear occur after 20-30 mins. After 4 h severe chest pain can occur, lasting for several hours. Other side effects include headache, increased blood pressure, tachycardia lasting several hours, nausea, vomiting, mydriasis, increased saliva and tear flow and perspiration. Greatly increased norepinephrine values have been shown (Fachinformation Yohimbin, "Spiegel"® 2008). Side effects may persist for 1-2 days (Tam et al., 2001). Instances of intoxication have been described at doses above 200 mg yohimbine HCl (yohimbine drug data sheet, "Spiegel"® , 2008). In one 16-year-old girl, 250 mg yohimbine brought about an overdose with dissociative reactions, weakness, paranoia, headache, nausea, chest pains, shivering, increased respiration rate, high blood pressure and tachycardia. The serum epinephrine and norepinephrine concentrations were increased. These symptoms persisted for 36 h (Linden et al., 1985). A dose of 1.8 g is reputed to have resulted in several hours' loss of consciousness (Wink et al., 2008). In a 37-year-old body builder, 5 g of yohimbine resulted in neurotoxic effects after 2 h. These

expressed themselves in nausea, vomiting and repeated episodes, hypertension (259/107 mmHg) and tachycardia. The plasma levels measured 3, 6, 14 and 22 h after intake were 5240, 2250, 1530 and 865 ng/ml (Giampreti et al., 2009).

Interactions of yohimbine HCl with alcohol and medication (antihypertensives, antidepressants and others) are known (McDougle et al., 1995; Fachinformation Yohimbin "Spiegel"®, 2008). Taking yohimbine HCl, particularly when combined with alcohol, can impair the ability to drive or operate machinery (Fachinformation Yohimbin "Spiegel"®, 2008).

The risk groups among which yohimbine HCl can have a more intense effect are people with cardiac impairment, hypertension, reduced renal and hepatic function, affective or paranoid psychiatric diseases and glaucoma (Fachinformation Yohimbin "Spiegel"®, 2008). Even normotensive subjects at risk of high blood pressure respond to yohimbine HCl with higher catecholamine values and increased blood pressure (Dao et al., 1998). Other studies do not give any indication that persons with high blood pressure or a tendency to orthostatic hypotension are particularly sensitive in their response to yohimbine (Tam et al., 2001). In patients with anxiety disorders, yohimbine triggers panic attacks in 50% of cases, while in healthy patients this only occurs in 5% of cases (Charney et al., 1984; Charney et al., 1987). According to the drug data sheet, women should not take yohimbine HCl, as the effect on sexual function disorders has not been subjected to adequate clinical investigation. No foetal effects of yohimbine HCl are known (yohimbine drug data sheet, "Spiegel"®, 2008).

c) Animal studies
Acute toxicity (oral LD50) in mice arises at less than 50 mg/kg body weight.
The LD50 for humans has been calculated as 5 mg/kg body weight (= 350 mg/70 kg body weight). The lethal dose is ten times higher (50 mg/kg). There are no data available for repeated or chronic use (Fachinformation Yocon-Glenwood®, 2005).

d) in vitro data
In vitro studies show that yohimbine is a selective and competitive α_2- adrenoreceptor antagonist with a low antagonist effect with regard to α_1-adrenoreceptors (Tam et al., 2001; HagerROM, 2006). Both of the metabolic products of yohimbine also bind to this receptor, but yohimbine has a higher binding affinity. In the presence of 5% albumin, the α_2-Adrenoreceptor binding affinity reduces 10-fold to that of its active metabolite 11-hydroxy-yohimbine. The plasma protein binding is 82%, 43% and 32% for yohimbine, 11-hydroxy-yohimbine and 10-hydroxy-yohibine (Berlan et al., 1993). 11-hydroxy-yohimbine is biologically active and has a capacity to block α_2-Adrenoreceptors in cells similar to that of yohimbine. Although 11- hydroxy-yohimbine has a lower binding affinity to α_2-adrenoreceptors than yohimbine, this is probably compensated by a significantly lower plasma protein binding (Berlan et al., 1993).

Other ingredients
In addition to yohimbine, yohimbe bark contains significant quantities of α-Yohimbine (rauwolscine). Both alkaloids largely conform in their profile of action. They selectively inhibit α-adrenoceptors with equal strength. Raubasine is an alkaloid which is chemically related to reserpine. It does not have a very pronounced anti-hypertensive effect. Raubasine is a selective α_1-adrenoreceptor antagonist and a prescription drug. Like yohimbine, yohimbinic acid selectively blocks the α_2-adrenoreceptors. The desirable and undesirable pharmacological effects correspond to those of yohimbine (HagerROM, 2006). Yohimbine is thus not the only pharmacologically relevant substance in yohimbe bark. It is not known to what extent

the effects of the individual substances influence one another. Matrix effects can also be expected from the tannin content of the bark, as these could precipitate the alkaloids (Khanbabaee and van Ree, 2001).

11. Characterisation of risk

There are no clinical data available on the **effects of Yohimbe bark** and preparations made from them.

The effects of **yohimbine HCl** vary widely from one individual to another. Huge variations between individuals are known with regard to the pharmacokinetics after oral administration of drugs which, like yohimbine HCl, are primarily metabolised through CYP2D6, and genetic variations for CYP2D6 with varying consequences have been described: defective alleles, alleles leading to a reduced metabolic rate, amplification of alleles with increased metabolic rate and changes to alleles with no functional consequences. The safety factor for substances primarily metabolised through CYP2D6 should accordingly be raised for inter-individual differences in toxicokinetics (Standard: 3.16) to 18, and in children even to 45 (Dorne et al., 2002). So far, it has not been possible to ascribe the high variability of the effect on the blood pressure to differences in the yohimbine metabolism or genetic variations in the α_2-adrenoreceptor (Le Corre et al., 2004; Etzel et al., 2005). Furthermore, the effects of the drug yohimbine HCl can only be transferred to yohimbe bark or extracts from the bark to a limited extent. Yohimbine HCl is more soluble in water than yohimbine, and the bark contains further pharmacologically active substances as well as tannins which can precipitate the alkaloids. The amount of yohimbine in yohimbe products vary greatly, and the results depend not just on the method of extraction, but also on the analytical method used.

Although yohimbine HCl is a prescription drug in Germany, and yohimbe bark is restricted to pharmacies, because of the claimed aphrodisiac and weight-reducing effect, **it can be assumed** that there is a market for products containing yohimbe bark.

Framework for action / measures

There are no clinical data available on the effects of Yohimbe bark. On the basis of the available data, the risk assessment of yohimbe bark and preparations made from it which place it at level **A**[9] **means that further data is necessary. To assess it at safety level B, the provision of clinical data on yohimbe bark and the relevant preparations is necessary.**

[9] European Food Safety Authority (2009) Guidance on Safety assessment of botanicals and botanical preparations intended for use as ingredients in food supplements.

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