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Soma, food of the immortals according to the Bower Manuscript (Kashmir, 6th century A.D.)☆

Marco Leonti [a,*], Laura Casu [b]

[a] Department of Biomedical Sciences, University of Cagliari, Via Ospedale 72, 09124 Cagliari (CA), Italy
[b] Department of Life and Environmental Sciences, University of Cagliari, Via Ospedale 72, 09124 Cagliari (CA), Italy

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ABSTRACT

Ethnopharmacological relevance: Food is medicine and vice versa. In Hindu and Ayurvedic medicine, and among human cultures of the Indian subcontinent in general, the perception of the food-medicine continuum is especially well established. The preparation of the exhilarating, gold-coloured Soma, Amrita or Ambrosia, the elixir and food of the 'immortals'–the Hindu pantheon–by the ancient Indo-Aryans, is described in the Rigveda in poetic hymns. Different theories regarding the botanical identity of Soma circulate, but no pharmacologically and historically convincing theory exists to date. We intend to contribute to the botanical, chemical and pharmacological characterisation of Soma through an analysis of two historical Amrita recipes recorded in the Bower Manuscript. The recipes are referred therein as panaceas (clarified butter) and also as a medicine to treat nervous diseases (oil), while no exhilarating properties are mentioned. Notwithstanding this, we hypothesise, that these recipes are related to the ca. 1800 years older Rigvedic Soma. We suppose that the psychoactive Soma ingredient(s) are among the components, possibly in smaller proportions, of the Amrita recipes preserved in the Bower Manuscript.

Materials and methods: The Bower Manuscript is a medical treatise recorded in the 6th century A.D. in Sanskrit on birch bark leaves, probably by Buddhist monks, and unearthed towards the end of the 19th century in Chinese Turkestan. We analysed two Amrita recipes from the Bower Manuscript, which was translated by Rudolf Hoernle into English during the early 20th century. A database search with the updated Latin binomials of the herbal ingredients was used to gather quantitative phytochemical and pharmacological information.

Results: Together, both Amrita recipes contain around 100 herbal ingredients. Psychoactive alkaloid containing species still important in Ayurvedic, Chinese and Thai medicine and mentioned in the recipe for 'Amrita-Prâsa clarified butter' and 'Amrita Oil' are: *Tinospora cordifolia* (Amrita, Guduchi), three *Sida* spp., *Mucuna pruriens*, *Nelumbo nucifera*, *Desmodium gangeticum*, and *Tabernaemontana divaricata*. These species contain several notorious and potential psychoactive and psychedelic alkaloids, namely: tryptamines, 2-phenylethylamine, ephedrine, aporphines, ibogaine, and L-DOPA. Furthermore, protoberberine alkaloids, tetrahydro-β-carbolines, and tetrahydroisoquinolines with monoamine oxidase inhibitor (MAO-I) activity but also neurotoxic properties are reported.

Conclusions: We propose that Soma was a combination of a protoberberine alkaloids containing *Tinospora cordifolia* juice with MAO-I properties mixed together with a tryptamine rich *Desmodium gangeticum* extract or a blending of *Tinospora cordifolia* with an ephedrine and phenylethylamine-rich *Sida* spp. extract. *Tinospora cordifolia* combined with *Desmodium gangeticum* might provide a psychedelic experience with visual effects, while a combination of *Tinospora cordifolia* with Sida spp. might lead to more euphoric and amphetamine-like experiences.

1. Introduction

The attempt of botanically identifying Soma, or the ingredients of soma-rasa, the ritual and intoxicating drink of the ancient Indo-Aryans, produced a wealth of theories and literature (e.g. Wasson, 1968; Falk, 1989; Flattery and Schwartz, 1989; McKenna, 1992;

☆"By this time the soma had begun to work. Eyes shone, cheeks were flushed, the inner light of universal benevolence broke out on every face in happy, friendly smiles" (Brave New World, Aldous Huxley, 1932).

* Corresponding author. Tel.: +39 0706758712; fax: +39 0706758553.
E-mail addresses: marcoleonti@netscape.net, mleonti@unica.it (M. Leonti).

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McDonald, 2004). Praised in the Rigveda as 'Soma' and in the Avesta as 'Haoma', both terms have their origin in the Indo-Iranian 'sau' meaning to "crush or grind by pressing with a pestle in a mortar" (Flattery and Schwartz, 1989, p.: 117). The Rigveda is the oldest text transmitted from the Vedic period, which lasted from approximately 1900 B.C. to around 1200 B.C. (Witzel, 1997). In the Vedas, Soma was simultaneously conceived of as a god, a plant, and as the earthly equivalent to Amrita ('non-death'–'a-mrta'), the celestial food of the immortals (see McDonald (2004)). The central geographic area of the Rigveda is the Punjab (Eastern Pakistan and North-western India), which coincides with what is generally regarded as the homeland of the Indo-Aryans (Witzel, 1987; McDonald, 2004).

Most commentators who approached the botanical identification of 'the' soma plant were tempted by the scarce hints at plant morphology occurring in the 9th book ('Mandala', Sanskrit: मण्डल) of the Rigveda (see for example: http://en.wikisource.org/wiki/The_Rig_Veda/Mandala_9). The contradictory and multi-interpretable metaphors and botanical allusions throughout the 114 hymns dedicated to Soma in the 9th Mandala, however, render an unambiguous botanical identification very difficult. In fact, the different commentators do not even agree whether Soma was an herb, a creeper, a tree or even a fungus. Hymn 96, verse 2 alludes to a climber or vine: "Men decked with gold adorn his golden tendril…". Hence, different commentators agreed that Soma was a vine or a climber. Srivastava (1954, p.: 26) writes that in the Rigveda soma "is described as a milky climbing plant, the juice of which was immensely liked by the celestial gods…" and that soma-rasa (the Soma juice) was prepared by pounding the entire creepers collected in the morning (p.: 28). Although Shrivastava gives no references he states that several authors suggested different botanical identification including *Sarcostemma acidum* (Roxb.) Voigt (Apocynaceae). Also Lewin (1973, p.: 216) mentions, amongst other species, two latex-bearing Apocynaceae as possible ingredients for Soma: *Periploca aphylla* Decne. (unresolved, Apocynaceae) and *Sarcostemma brevistigma* Wight & Arn. (=*Sarcostemma acidum* (Roxb.) Voigt, Apocynaceae). Milk plays indeed an important role in the preparation of Soma but there are no clues that the soma plant itself had a milky juice or latex. Rather it appears that a golden or yellow (also red-brownish) watery plant juice produced with the help of pressing stones, was either first blended with milk and then cleansed by means of a fleece or sheep's wool or that the juice was first cleansed and then blended with milk and subsequently mixed with a sort of oil:

Rigveda, Mandala 9, hymn 101, verse 11: "Effused by means of pressing-stones…" h. 101, v. 12: "These Soma juices, skilled in song, purified, blent with milk and curd, when moving and when firmly laid in oil, resemble lovely suns". H. 69, v. 9: "…effused, they pass the cleansing fleece, while, gold-hued, they cast their covering off to pour the rain down." H. 72, v. 1: "They cleanse the gold-hued: like a red steed is he yoked, and Soma in the jar is mingled with the milk." H. 103, v. 2: "Blended with milk and curds he flows on through the long wool of the sheep." H. 107, v. 26: "Urged onward by the pressers, clad in watery robes, Indu is speeding to the vat." H. 8, v. 6: "When purified within the jars, Soma, bright red and golden-hued, hath clothed him with a robe of milk." H. 109, v. 21: "…they cleanse thee for the gods, gold-coloured, wearing water as thy robe." H. 107, v. 10: "Effused by stones, o Soma, and urged through the long wool of the sheep, thou, entering the saucers as a man the fort, gold-hued hast settled in the wood." H. 31, v. 5: "For thee, brown-hued! the kine have poured imperishable oil and milk." H. 98, v. 7: "Him with the fleece they purify, brown, golden-hued, beloved of all, who with exhilarating juice goes forth to all the deities". H. 78, v. 4: "He whom the gods have made a gladdening draught to drink, the drop most sweet to taste, weal-bringing, red of hue." H. 107, v. 4: Cleansing thee, Soma, in thy stream, thou flowest in a watery robe: Giver of wealth, thou sittest in the place of law, o god, a fountain made of gold." (See: http://en.wikisource.org/wiki/The_Rig_Veda/Mandala_9).

Flattery and Schwartz report that *Sarcostemma acidum* is one of the plants used today by Brahmans as a substitute for the ancient Soma and also Padhy and Dash (2004) have gathered anecdotal evidence that in some parts of India a sort of soma ritual is still being practiced employing *Sarcostemma acidum*, which, however, does not have the capacity to alter one's state of mind. This results in the paradoxical situation that, while in present day soma rituals the recited liturgies allude to the intoxicating effects of the potion, the plants used in contemporary settings lack any intoxicating properties (Flattery and Schwartz, 1989, p.: 4). In fact, the hymns in the 9th Mandala of the Rigveda speak of "granter of bliss" (h. 1, v. 3), "runs forth to the luminous realm of heaven" (h. 37, v. 3), "rapturous joy" (h. 45, v. 3), "bring us all felicities" (h. 62, v. 1), "bringing wisdom and delight" (h. 63, v. 24), "light that flashes brilliantly" (h. 64, v. 28) "gladdening draught to drink" (h. 78, v. 4), or "exhilarating juice" (h. 98, v. 7). Flattery and Schwartz (1989) defend the opinion that the botanical identity of 'Haoma' in the Iranian traditions as well as that of 'Soma' of the Hindu traditions is the Syrian rue (*Peganum harmala* L., Nitrariaceae) containing harmala alkaloids with monoamine oxidase inhibitory (MAO-I) activity. Falk (1989) on the other hand argues that "there is no need to look for a plant other than *Ephedra* for the original Soma" since ephedrine (**30**) containing *Ephedra* spp. are referred to as 'hum', 'hom', 'som' or 'soma' in different languages and because the Parsi in Iran still use *Ephedra* sp. in their Haoma ritual. Hints from the artistic and mythic wealth of India and southeast Asia led McDonald (2004) to hypothesise that the botanical identity of Soma is to be found in the 'eastern' or 'sacred' lotus (*Nelumbo nucifera* Gaertn., Nelumbonaceae). The sacred lotus is not only a highly symbolic plant associated with Hindu and Buddhist gods (McDonald, 2004) but also an important food and medicinal plant (Mukherjee et al., 2009).

We argue that focusing on the identification of a single "soma species" or single soma recipe contributed much to the inconsistencies present in the different identification attempts and the apparent contradictions between the proposed theories and botanical species. In this contribution we attempt to circumscribe the plant species that come into consideration for the preparation of Soma and try to identify Soma's botanical identity. Systematic and multidisciplinary botanical and medico-therapeutic analyses of ancient medical scripts and herbal books can help to provide more verified insights into the history and evolution of plant use (Leonti, 2011). We assume that over the course of time the Soma recipe evolved and that more than only one soma recipe existed and that Soma was a more or less complex herbal drug formulation including different species, some more symbolic, some less indispensable for the mind-altering effect, than others. Our attempt of botanically identifying soma is based on the analysis of two herbal formulations reported in the so-called "Bower Manuscript" referred therein as (**I**) "Amrita-Prâsa clarified butter" (Hoernle, 2011, p.: 90–91) and (**II**) "Amrita Oil" (Hoernle, 2011, p.: 106–107).

2. The Bower Manuscript

The Bower Manuscript (BM) was dug out from a man-made, mound-like construction called 'stûpa' close to the underground city of Ming-oï-Qumturâ, 16 miles west from Kuchar (Hoernle, 2011, p.: iv). Kuchar is an oasis settlement with a Buddhist history situated on the Silk Road in Eastern Turkestan (China) north of Takla Makan. The manuscript is named after Lieutenant Hamilton Bower, who acquired the script in Kuchar in 1890 (Hoernle, 2011). The BM is written in, as Rudolf Hoernle [1841–1918] calls it, ungrammatical Sanskrit, a mixture of literary and popular Sanskrit. The script used throughout the manuscript is known as the 'Gupta' script coinciding with the era of the

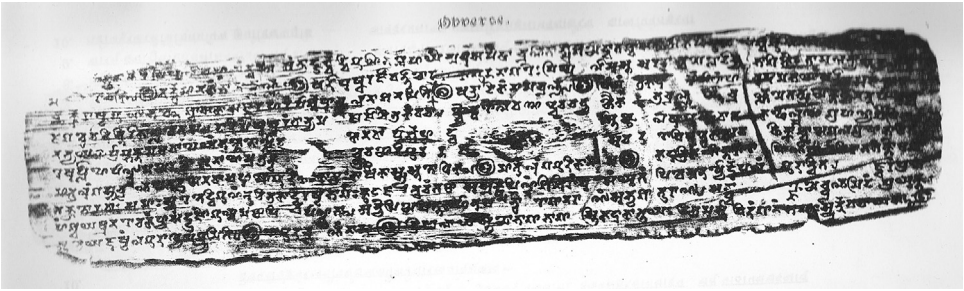


Fig. 1. Pôthi of the Bower Manuscript, taken from Hoernle (2011, Plate VII).

Gupta Empire [300–550 A.D.] of northern India (p.: xxvi). Remarkably, the BM is the hitherto oldest known original medical treatise from the Indian subcontinent (Hoernle, 2011, foreword and p.: lxviii). Written by four different authors (p.: xxxvii) on birch bark leaves (cut from periderm of *Betula utilis* D. Don (Betulaceae)), the BM is actually a collection of seven separate manuscripts originally presented in the form of a 'pôthi' (Fig. 1; p.: xvii) a collection of loose leaves in-between two wooden boards held together "by a string which passes through a hole drilled through the whole pile" (p.: xvii). Pôthis seem to be South Indian in origin, since the palm-leaf of *Corypha umbraculifera* L. (Arecaceae) was the original writing support of pôthis and thereby also determined their overall shape (p.: xviii). Himalayan birch, (*Betula utilis*) is native only to Kashmir and Udyâna in the North of India (p.: xx). The writing style and the fact that the authors used birch bark for their records led Hoernle to conclude that the scribes of parts I–III and parts V–VII, most probably Buddhist monks, migrated from an unknown location in India via Kashmir or Urdyâna to Kuchar, where they finally manufactured the manuscripts.

Through a comparative analysis of particularities in the script-style of the BM, Sander (1987) argues that especially parts I–III contain elements typical for ancient Kashmiri scripts and that the BM is in reality a product of Kashmir itself. Sander (1987) provides also evidence suggesting that the BM was written between the beginning and the middle of the sixth century A.D. shifting the date of origin proposed by Hoernle around 150 years towards the present and towards the end of the Gupta Empire. According to Hoernle (p.: xxxvi), the author of part II, which contains the two recipes that are the object of this analysis, probably came from the northern fringe of the northern part of the Indian 'Gupta script' area (Hoernle, p.: xxxvi).

3. Methods

The plant species contained in both formulations, the "Amrita-Prâsa clarified butter" (**I**) and the "Amrita oil" (**II**), botanically identified by Hoernle (2011) through an analysis of their Sanskrit names and provided with Latin binomials were cross-checked with theplantlist.org (http://www.theplantlist.org/) for synonyms and their accepted contemporary Latin binomials. The updated Latin binomials appear framed in square brackets in recipes **I** (4.1.) and **II** (4.2.).

A literature search focusing on psychoactive secondary metabolites and associated pharmacologic effects was performed with the updated Latin binomials and the help of search engines such as Scopus and Pubmed. Special attention was given to quantitative phytochemical analyses.

4. Recipes

4.1. (I) The Amrita-Prâsa clarified butter (Hoernle, 2011, pp.: 90–91).

The numbers in brackets refer to the ślôka [sûtras], see also Srivastava (1954, p.: 153), while the superscript numbers are identical to Hoernle's text and refer to notes therein.

"The Amrita-Prâsa Clarified Butter,[55] in 11 ślôka and 1 pâda. (Verses 108-119*a*.). I will now describe the ambrosia-like elixir, which increases the strength of men, the so-called Amrita-prâśa (or Food of the Immortals), a most noble *kind of* clarified butter. (109) Take one prastha each of the juice of emblic myrobalan [*Phyllanthus emblica* L., (Phyllanthaceae)], Kshîravidârî (*Ipomoea digitata*) [*Ipomoea cheirophylla* O'Donell, (Convolvulaceae)] and sugar cane [*Saccharum officinarum* L., (Poaceae)], and similarly of the milk of a heifer (110) one prastha, and add one well-measured prastha of fresh clarified butter. Throw in, also, pastes[33] made of one half pala each of the following drugs: (111) Rishabhaka[56] [unknown and substituted], Riddhi[56] [unknown and substituted], liquorice [*Glycyrrhiza glabra* L., (Fabaceae)], Vidârigandhâ (*Desmodium gangeticum*) [*Desmodium gangeticum* (L.) DC., (Fabaceae)], *Payasyâ (*Gynandropsis pentaphylla*) [*Cleome gynandra* L., (Cleomaceae)], Sahadêvâ (*Sida rhomboidea*) [*Sida rhombifolia* L., (Malvaceae)], Anantâ (*Hemidesmus indicus*) [*Hemidesmus indicus* (L.) R. Br. ex Schult., (Apocynaceae)], Madhûlikâ (*Bassia latifolia*) [*Madhuca longifolia* (J. König ex L.) J.F. Macbr., (Sapotaceae)] and Viśvadêvâ (*Sida spinosa*) [*Sida spinosa* L., (Malvaceae)], (112) both Mêdâ[56] [unknown and substituted], Rishyaprôktâ (*Sida cordifolia*) [*Sida cordifolia* L., (Malvaceae)], Śatâvarî (*Asparagus racemosus*) [*Asparagus racemosus* Willd., (Asparagaceae)], Mudgaparnî (*Phaseolus trilobus*) [*Vigna trilobata* (L.) Verdc., (Fabaceae)] and Mâshaparnî (*Teramnus labialis*) [*Teramnus labialis* (L. f.) Spreng., (Fabaceae)], Śrâvanî (*Sphaeranthus indicus*) [*Sphaeranthus indicus* L., (Asteraceae)], cowhage [*Mucuna pruriens* (L.) DC., (Fabaceae)] and Vîrâ (*Uraria lagopodioides*) [*Uraria lagopodoides* (L.) DC., (Fabaceae)]. (113) Further add one kudava each of raisins [*Vitis* sp., (Vitaceae)], dates [*Phoenix dactylifera* L., (Arecaceae)], jujubes [*Ziziphus jujuba* Mill., (Rhamnaceae)], and half as much each of walnuts [*Juglans regia* L., (Juglandaceae)], Tinduka (*Diospyors Embryopteris*) [*Diospyros atrata* (Thwaites) Alston *or Diospyros albiflora* Alston, (Ebenaceae)] and Nikôchka (*Alangium decapetalum*) [*Alangium salviifolium* (L.f.) Wangerin, (Cornaceae)].

(114) Having boiled and strained *the whole*, let it stand in a clean vessel, *and* when it has cooled, add one prastha of well-clarified honey, (115) and sixteen pala of choice white sugar. Then take one half pala of black pepper [*Piper nigrum* L., (Piperaceae)] and one

pala of small cardamoms [*Elettaria cardamomum* (L.) Maton, (Zingiberaceae)] (116) powder them finely, and, having sprinkled them *over the whole*, stir it with a ladle. Of this *preparation* a dose suited to the *patient's* power of digestion may be administered, (117) and when it is digested, rice-milk, together with the broth of the flesh of land-animals, may be given. This Amrita-prâśa is an excellent preparation for increasing the strength and colour of men; (118) it may be given in cases of weakness induced by consumption or ulcers, also to the old, the feeble and the young, also to those who are suffering from fainting, asthma, and hiccough. (119*a*) This *preparation of* clarified butter, being a composition of Âtrêya's, is famed under the name Amrita (or 'ambrosia')."

Hoernle states[(55)] that this formula, although with more ingredients and different proportions, occurs also in the Charaka VI and Âshtânga Hridaya IV. Hoernle[(56)] mentions that the eight drugs known to the ancients and now substituted are: 1. Jîvaka, 2. Rishabha, 3. Mêdâ, 4. Mahâmêdâ, 5. Kâkôlî, 6. Kshîra-kâkôlî, 7. Riddhi, 8. Vriddhi; 1 and 2: Root of Vidârî (*Batatas paniculata* [*Ipomoea mauritania* Jacq, (Convolvulaceae)]) 3 and 4: Roots of Śatâvarî (*Asparagus racemosus* [*Asparagus racemosus* Willd., (Asparagaceae)]) 5 and 6: Aśhvagandhâ (*Withania somnifera* [*Withania somnifera* (L.) Dunal, (Solanaceae)]), 7 and 8: Tubers of the Varâhî or Bhadramustra (*Cyperus pertenuis* [*Cyperus articulatus* L. or *C. tenuiflorus* Rottb., (Cyperaceae)]).

4.2. (II) The Amrita Oil (Hoernle, 2011, pp.: 106–107):

"(IV) The Amrita Oil,[116] in 25 ślôka and 1 pâda. (287–312*a*.) The two truth-speaking Aśvins, the divine physicians, honoured by the Dêvas, have declared the following excellent health-promoting oil, (288) which relieves all diseases, is fit for a king, and is as good as ambrosia. It is known by the name of Amrita (or 'ambrosia'), and is an oil able to make men strong. (289) At the time of Pushya[117], after having said prayers[118], performed purification rites, and asked the Brâhmans' blessing in a few words, take out liquorice-roots grown in a favourable place. (290) Of the fresh juice of these roots take four pâtra[9], and add four pala each of *the following drugs*: Papaundarîka[119] [a fragrant wood], Amritâ (*Tinospora cordifolia*) [*Tinospora cordifolia* (Thunb.) Miers, (Menispermaceae)], knots of lotus-stalks [*Nelumbo nucifera* Gaertn., (Nelumbonaceae)], Śatâvarî (*Asparagus racemosus*) [*Asparagus racemosus* Willd., (Asparagaceae)], (291) Śringâtaka (*Trapa bispinosa*) [*Trapa natans* var. *bispinosa* (Roxb.) Makino, (Lythraceae)], emblic myrobalan [*Phyllanthus emblica* L., (Phyllanthaceae)], Undumbara (*Ficus glomerata*) [*Ficus racemosa* L., (Moraceae)], Kaśêruka (*Scripus Kysoor*) [*Actinoscirpus grossus* var. *kysoor* (Roxb.) Noltie, (Cyperaceae)], the bark of each of the (five) trees with a milky sap[120] [Nyagrôdha (Ficus indica) [*Ficus* sp., (Moraceae)], Udumbara (*Ficus glomerata*) [*Ficus racemosa* L., (Moraceae)], Asvattha (*Ficus religiosa*) [*Ficus religiosa* L., (Moraceae)], Plaksha (*Ficus infectoria*) [*Ficus* sp., (Moraceae)], Pârîsha (*Thespesia populnea*) [*Thespesia populnea* (L.) Sol. ex Corrêa, (Malvaceae)], (292) roots of Kuśa (*Poa cynosuroides*) [*Desmostachya bipinnata* (L.) Stapf, (Poaceae)], Kâsa (*Saccharum spontaneum*) [*Saccharum spontaneum* L., (Poaceae)] and Ikshu (*Saccharum officinarum*) [*S. officinarum* L., (Poaceae)], also of Śara (*Saccharum Sara*) [*Saccharum bengalense* Retz., (Poaceae)] and Vîrana (*Andropogon muricatus*)[121] [*Chrysopogon zizanioides* (L.) Roberty, (Poaceae)], also roots of Gundrâ (*Panicum uliginosum*) [*Sacciolepis interrupta* (Willd.) Stapf, (Poaceae)], of Nadikâ[122] [not identified] and of the lotus [*N. nucifera*], (293) Vadarî (*Ziziphus Jujuba*) [*Z. jujuba*], Vidârî (*Ipomoea digitata*) [*I. cheirophylla*], Vêtasa (*Calamus Rotang*) [*Calamus rotang* L., (Arecaeea)], Adurûshaka (*Adhatoda vasica*) [*Adhatoda vasica* Nees, unresolved (Acanthaceae)], Nîm [*Azadirachta indica* A. Juss., (Meliaceae)], Sâlmalî (*Bombax malabaricum*) [*Bombax ceiba* L., (Malvaceae)], dates [*P. dactylifera*], cocoanut [*Cocos nucifera* L., (Arecaceae)], Priyangu (*Aglaia Roxburghiana*) [*Aglaia elaeagnoidea* (A. Juss.) Benth., (Meliaceae)], (294) Patôla (*Trichosanthes dioica*) [unresolved ev. *Mukia maderaspatana* (L.) M.Roem, (Cucurbitaceae)], Kutaja (*Holarrhena antidysenterica*) [*Wrightia antidysenterica* (L.) R.Br. or *Holarrhena pubescens* Wall. ex G. Don, (Apocynaceae)], raisins [*Vitis* sp.], leaf-stalk of the lotus [*N. nucifera*], sandal [*Santalum* sp., (Santalaceae)], Kakubha (*Terminalia Arjuna*) [*Terminalia arjuna* (Roxb. ex DC.) Wight & Arn., (Combretaceae)], Aśvakarna (*Shorea robusta*) [*Shorea robusta* Gaertn., (Dipterocarpaceae)], Lâmajjaka (*Adropogon laniger*) [*Cymbopogon jwarancusa* subsp. *olivieri* (Boiss.) Soenarko, (Poaceae)], and plumbago-root [*Plumbago zeylanica* L., (Plumbaginaceae)], (295) also other astringent, sweet or cooling drugs, as many as may be obtainable. Boil all these in two drôna of water, (296) and when *the whole* is reduced to one-eight *of the original quantity*, boil in it pastes made of fine powder of one pala each of the following drugs: Balâ (*Sida cordifolia*) [*Sida cordifolia* L., (Malvaceae)], Nâgabalâ (*Sida spinosa*) [*Sida spinosa* L., (Malvaceae)], Jîvâ (*Dendrobium multicaule*) [*Conchidium muscicola* (Lindl.) Rauschert, (Orchidaceae)], cowhage [*M. pruriens*], Kasêruka (*Scirpus Kysoor*) [*A. grossus* var. *kysoor*], (297) Nata (*Tabernaemontana coronaria*) [*Tabernaemontana divaricata* (L.) R.Br. ex Roem. & Schult., (Apocynaceae)], juice of sugar-cane[123], Sprikkà (*Trigonella corniculata*) [*Trigonella balansae* Boiss. & Reut., (Fabaceae)], small cardamoms [*E. cardamomum*] and cinnamon-bark [*Cinnamomum* sp., (Lauraceae)], Jîvaka[56] [unknown and substituted] Rishabhaka[56] [unknown and substituted] Mêdâ[56] [unknown and substituted], Madhuka (*Bassia latifolia*) [*M. longifolia* var. *latifolia*, (Sapotaceae)], and blue lotus [*Nymphaea nouchali* var. *caerulea* (Savigny) Verdc., (Nymphaeaceae)] (298), the colour producing saffron [*Crocus sativus* L., (Iridaceae)], aloe-wood [*Aquilaria* sp., (Thymelaeaceae)], and cinnamon-leaves [*Cinnamomum* sp.], Vidârî (*Ipomoea digitata*) [*I. cheirophylla*], Kshîrakakôlî[63] [said to be unknown], Vîrâ (*Uraria lagopoides*) [*Uraria lagopodoides* (L.) DC., (Fabaceae)], and Śârivâ (*Ichnocarpus frutescens*) [*Ichnocarpus frutescens* (L.) W.T. Aiton, (Apocynaceae)], (299) Śatâvarî (*Asparagus racemosus*) [*A. racemosus*], Priyangu (*Aglaia Roxburghiana*) [*A. elaeagnoidea*], Gudûchî (*Tinospora cordifolia*) [*Tinospora cordifolia*], filaments of the lotus [*N. nucifera*], Lâmajjaka (*Andropogon laniger*) [*C. jwarancusa* subsp. *olivieri*], red and white sandal [*Santalum* spp.], and fruits of Râjâdana (*Mimusops hexandra*) [*Manilkara hexandra* (Roxb.) Dubard or *Mimusops coriacea* (A.DC.) Miq., (Sapotaceae)], (300) pearl, coral, conch-shell, moon-stone, sapphire, crystal, silver, gold, and other gems and pearls, (301) liquorice [*G. glabra*], madder [*Rubia tinctorum* L., (Rubiaceae)], and Amśumatî (*Desmodium gangeticum*) [*Desmodium gangeticum*]. Boil *the whole* slowly over a gentle fire (302) with four pâtra of (sweet) oil and eight times as much of milk, adding also tamarind-juice [*Tamarindus indica* L., (Fabaceae)] and vinegar of rice[124] one half as much as the milk. (303) This boiling should be repeated a hundred or even a thousand times; and when it is thoroughly done, it may be known by this sign, (304) that on the approach of the proper time the oil stiffens by *exposure to* the rays of the sun.[125] After asking the Brâhmans' blessing, performing purificatory rites and saying prayers, (305) this Amrita (or 'ambrosial') oil, highly esteemed by the Dêvas, may be administered *to the patient*, in the form of an injection per anum or per urethram,[110] or as a draught, or an errhine, or a liniment.

(306) It serves the purpose of relieving disease and imparting strength to the organs of sense. For those who suffer from morbid heat and thirst it makes an excellent and beneficial liniment. (307) It promotes the growth of the hair in the old and

that of the body in the young; it produces loveliness and grace in women; and also *ensures* numerous offspring, (308) for, by the use of this ambrosial oil, women are predisposed to conception. It cures the eighty nervous diseases[109], also those due to *derangement of* the blood or the bile (309) or the phlegm or all the humours concurrently.[126] By its use as an errhine or a liniment the eyes become as sharp as those of an eagle. (310) It keeps of calamities, averts all fortune, and promotes prosperity. By the use of this oil the Maharshi Chyavana[92] regained (311) his youth, and was delivered from decrepitude and disease; and the blessed Maharshi Mârkandêya[127], who was desirous of a long life, (312*a*) obtained his desire by the regular use of this oil."

Hoernle(116) was not able to find this formula elsewhere and notes that it is a "phenomenally long one" containing 83 ingredients. Hoernle(9) gives some explanations on the measures and states that pâtra is also called âdhaka. Paramhans (1984) explains the medieval Indian weight measurement system as follows: 2 pala = 1 prasrti, 2 prasrtis = 1 añjali or kudava, 2 añjalis = 1 śaravâ, 2 śaravâs = 1 prastha, 4 prasthas = 1 âdhaka, 4 âdhakas = 1 drôna. Since over the course of time the overall mass changed but the proportions within the Indian weight measurement system remained the same, a translation into Western weight equivalents makes no sense.

5. Theoretical frame of the research question

What at first sight caught our attention were the names of the two recipes along with the description of "good as ambrosia" or "ambrosia-like elixir". 'Amrita' means 'immortality' and is a synonym of Soma, 'Amrita-prâsa' means 'food of the immortals' and 'ambrosia' can be translated as 'food of the gods' or 'nectar'. While we use here Amrita as a synonym of Soma, nothing about the description of the recipes, not even the therapeutic indications, suggest or allude to any exhilarating, intoxicating or psychoactive property of 'Amrita clarified butter' or 'Amrita oil'. However, the 'Amrita oil' is also said to cure "the eighty nervous diseases" (p.: 107). As further reading on the ethnomedical concept of nervous diseases Hoernle(119) indicates the commentary on the Hindu system of medicine by Wise (1845) as well as the Bhâva Prakâśa and the Charaka Samhitâ, both edited by Pandit Jibananda V. at Calcutta in 1875 and 1877, respectively. Due to external forces (e.g. dryness, cold, light types of food, wet cloths), physical overstraining (e.g. excessive sexual practice, improper exercise) or psychological reasons (too much thinking, sorrow, grief, fear, anger) air is deranged, which causes different kind of symptoms, such as: "persons speak nonsense", "affected parts shake", "pain in the chest, head and temples", body is "bent like a bow", "spasmodic convulsions", "difficulties in breathing", "person cannot speak", "dyspepsia and drowsiness", "trembling and shivering", "head is always shaking" (Wise, 1845, pp.: 250–258). Moreover, 'Amrita-prâsa' as well as 'Amrita oil' are said to relieve all diseases and to "increase the strength of men" or "make men strong". The term 'men' in the text evidently refers to men *and* women since the Amrita oil is reported to produce "loveliness and grace in women" and to predispose women to conception.

The original Soma rite, central to which was the taking of a psychoactive Soma potion conferring the participants a god-like perspective, came into disuse but neither is it clear when exactly the Soma rite was abandoned nor what was its cause or reason. Besides the cultural transition taking place towards the end of the Rigvedic period, neurotoxic side effects of the Soma potion might have conditioned the loss of the Soma rite. A Soma (Amrita) recipe written down in the 6th century A.D., around 1800 years after the demise of the Rigvedic period can be expected to have received modifications in its formulation as well as in its medico-therapeutic application. The evolution of the Amrita recipes possibly affected the number of ingredients, proportions, overall indications and therapeutic use as well as the medico-philosophical frame. Although the evolution of these aspects evades a closer scientific analysis we argue that if these two recipes are derivatives of an ancient Soma formulation (or formulations), the core species required for the induction of a psychoactive effect should, eventually in smaller proportions, be present among the ingredients. In more general terms we argue that the Soma plant(s), so central to the Indo-Aryan culture, did not vanish from the Indian herbal scenery but linger on in herbal medicine as genuine medicinal plants.

6. Research questions

(i) Are there plant species among the ingredients of the two recipes able, either in combination or alone, to induce mind-altering effects upon ingestion?
(ii) If so, is the concentration of central nervous system (CNS) active compounds in the species under examination sufficient in order to induce perceivable pharmacologic effects? i.e. is the processing and practical application of the quantity of (crude) drugs needed to induce perceivable pharmacologic effects feasible? This includes that the potentially psychoactive constituents should not only be present at physiologically relevant amounts in the plant material but also be bio-available and extractable with water or an emulsion such as milk in reasonable quantities. Moreover, should a suggestion that makes practical sense also consider bio-geography and the theoretical availability of the species in the region of the Punjab.
(iii) A more specific question relates to the pharmacology of the formulations and if they contain monoamine oxidase (MAO) substrates and/or MAO inhibitors (MAO-I):

Are there neurotransmitter mimicking MAO substrates (possibly easy extractable alkaloids) as well as secondary metabolites able to interrupt the catabolic MAO pathways present in the species listed among the ingredients of recipe **I** and **II**?

The pharmacologic potentiation resulting from a combination of tryptamines with MAO inhibiting β-carbolines has been described for South American snuffs (Holmstedt and Lindgren 1967, p.: 365) and Ayahuasca (Callaway et al., 1999). Such a potentiation of pharmacologic effects can theoretically also be achieved with the β-carboline containing *Peganum harmala* seeds (see theory put forward by Flattery and Schwartz for Haoma).

7. Results

7.1. Analysis of the two recipes

A comparison of the ingredients of the two recipes shows that only few species make part of both formulations namely: *Asparagus racemosus*, *Phyllanthus emblica*, *Ipomoea cheirophylla*, *Mucuna pruriens*, *Sida spinosa*, *Sida cordifolia*, *Madhuca longifolia*, *Uraria lagopodoides*

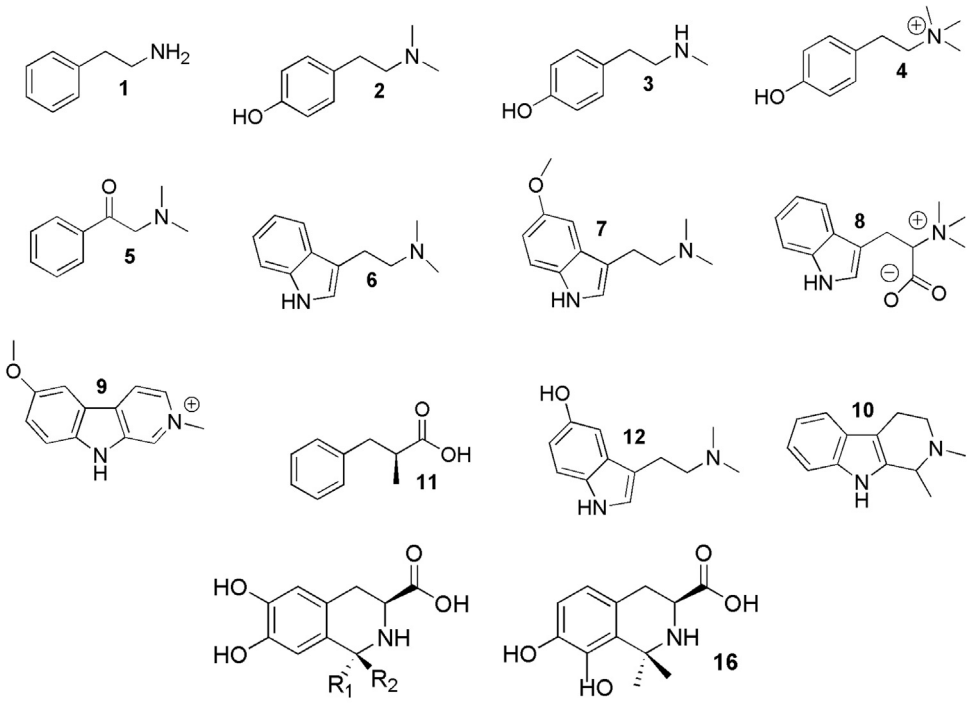
and *Desmodium gangeticum*. Species with potentially psychoactive metabolites detected in recipe (**I**) are: *Sida spinosa*, *Sida cordifolia*, *Sida rhombifolia*, *Mucuna pruriens* and *Desmodium gangeticum*. An analysis of recipe (**II**) revealed the following species with potentially psychoactive metabolites: *Sida spinosa* and *Sida cordifolia*, *Mucuna pruriens*, *Desmodium gangeticum*, *Nelumbo nucifera*, *Tinospora cordifolia*, *Tabernaemontana divaricat*a. Neither *Ephedra* spp. nor *Peganum harmala* have been identified by Hoernle (2011) among the different recipes reported in the BM. Notably, the recipes do not contain any clear indication regarding the dose at which the mixtures should be applied for the treatment of the various health conditions and purposes for which they are recommended.

7.2. Species with potentially psychoactive metabolites detected in recipes I and II and their main constituents

7.2.1. Desmodium gangeticum (Fabaceae)

Desmodium gangeticum is a prostrate to sub-erect perennial weed growing throughout the Indian subcontinent in hilly areas up to 1500 m a.s.l. Under favourable conditions the plant can reach several metres in height (Ramakrishnan, 1964). The herb is called 'salpan' or 'salpani' in Hindi and 'shalaparni', 'amśumatî' or 'vidârigandhâ' in Sanskrit and is an important medicinal species within the Ayurvedic system of medicine (Hoernle, 2011; Rastogi et al., 2011). Chemical evaluations of above and below-ground tissues of *Desmodium gangeticum* by Banerjee and Ghosal (1969), as well as by Ghosal and Bhattacharya (1972) revealed the presence of different *β*-phenethylamines (2-phenylethylamine (PEA, **1**), hordenine (**2**), *N*-methyltyramine (**3**), candicine (**4**), *N*,*N*-dimethyl-2-oxo-2-phenylethylamine (**5**)), indolylalkylamines (*N*,*N*-dimethyltryptamine (DMT, **6**) and its N_b-oxide, 5-methoxy-*N*,*N*-dimethyltryptamine (5-MeO-DMT, **7**) and its N_b-oxide and hypaphorine (**8**)) and *β*-carbolines (6-methoxy-2-methyl-*β*-carbolinium cation (**9**) and 1,2-dimethyl-2,3,4,9-tetrahydro-1H-*β*-carboline (1,2-Me-THBC, **10**)).

From 1 kg fresh above ground plant material Banerjee and Ghosal (1969) obtained the following quantities of alkaloids: From the aqueous acidic extract (derived from the extracted chloroform layer) basified with ammonia and extracted with chloroform: 5-MeO-DMT (570 mg), DMT (not quantified), DMT-N_b-oxide (210 mg) and 5-MeO-DMT-N_b-oxide (180 mg). The chloroform soluble acetates were identified as N_b-methyltetrahydroharman (1,2-Me-THBC, 30 mg), DMT (410 mg) and DMT-N_b-oxide (120 mg), while from the aqueous mother liquor 210 mg of 6-methoxy-2-methyl-*β*-carbolinium cation was obtained. Altogether more than 1730 mg of alkaloids were extracted from 1 kg of fresh plant material and Banerjee and Ghosal (1969) note that dried plant material contains higher proportions of 5-MeO-DMT with respect to fresh material.

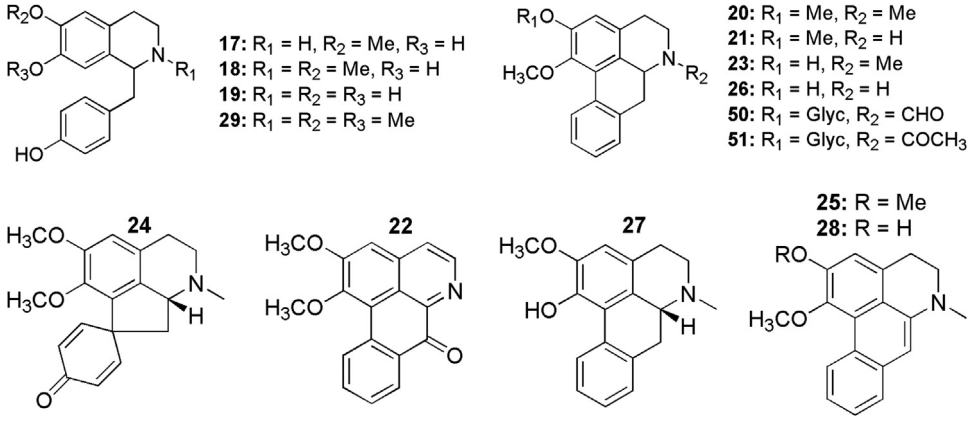


7.2.2. Mucuna pruriens (Fabaceae)

Mucuna pruriens is an annual herb growing throughout the Indian plains and cultivated as a vegetable and fodder called 'kavach' in Hindi and 'atmagupta' or 'vanari' in Sanskrit (Williamson, 2002; Misra and Wagner, 2004). The seeds of *Mucuna pruriens* contain high amounts of L-DOPA (L-3,4-dihydroxyphenylalanine, **11**). Mahajani et al. (1996) quantified the L-DOPA content of 10 g dried *Mucuna pruriens* seeds at around 330 mg, while Raina and Khatri (2011) found L-DOPA concentration in dried seeds of different accessions to vary considerably from 2.2 to 5.3% of dry weight. From the pods, seeds, leaves and roots several indole-3-alkylamines including DMT (**6**), DMT-N_b-oxide, bufotenine (5-OH-DMT, **12**), 5-MeO-DMT (**7**), two not closer characterised 5-oxyindole-3-alkylamines and one *β*-carboline were isolated (Ghosal et al., 1971). Misra and Wagner (2004) furthermore report on the isolation of four 1,2,3,4-tetrahydroisoquinoline alkaloids (**13-16**, 94 mg altogether) from 500 g dried seeds.

7.2.3. Nelumbo nucifera (Nelumbonaceae)

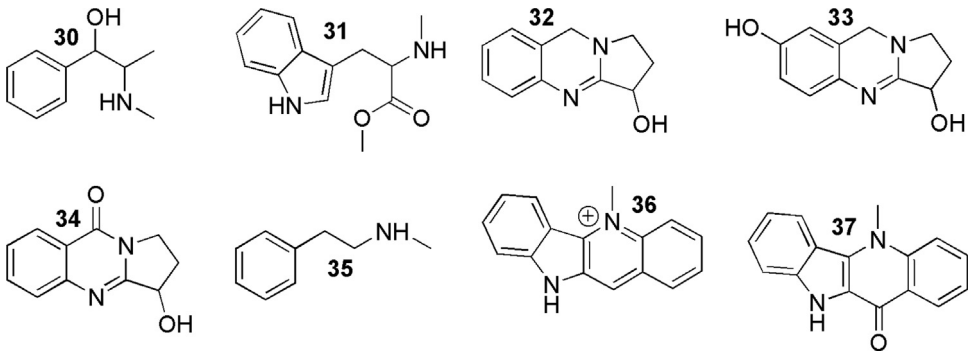
The natural distribution of *Nelumbo nucifera* ranges from the Caspian Sea to eastern Asia (McDonald, 2004), while Holm et al. (1979, p.: 246) list *N. nucifera* as a weed for India. The species is known in India as 'lotus', 'kamala' or 'padma' (Mukherjee et al., 2009). From the seeds, flower buds and the leaves a range of benzyltetrahydroisoquinolines, bisbenzylisoquinolines and aporphine type alkaloids have been isolated (Kunitomo et al., 1973; Shoji et al., 1987; Sugimoto et al., 2010; Nakamura et al., 2013). For a comprehensive review on the phytochemical constituents of the different lotus tissues see Mukherjee et al. (2009). From 3 kg of dried *Nelumbo nucifera* leaves Kashiwada et al. (2005) obtained 275 mg (+)-(*R*)-coclaurine (**17**), 28 mg (-)-1(*R*)-*N*-methylcoclaurine (**18**) and 507 mg of (-)-1(*S*)-norcoclaurine (**19**). From the EtOAc fraction of 1 kg flower buds Nakamura et al. (2013) extracted nuciferine (**20**, 148 mg), *N*-nornuciferine (**21**, 11.2 mg), lysicamine (**22**, 36.5 mg) and from the butanol fraction *N*-methylasimilobine (**23**, 6.6 mg), lysicamine (102 mg) and pronuciferine (**24**, 56.0 mg). From the EtOAc fraction of 900 g powdered leaves *N*-methylasimilobine-*N*-oxide (3.3 mg), nuciferine (67.3 mg) nuciferine-*N*-oxide (40.7 mg), *N*-nornuciferine (2.3 mg), dehydronuciferine (**25**, 3.9 mg), lysicamine (41.8 mg) and from the butanol fraction nuciferine (83.0 mg), nuciferine *N*-oxide (22.1 mg), *N*-methylasimilobine (282 mg), asimilobine (**26**, 149 mg), (-)-lirinidine (**27**, 7.2 mg), 2-hydroxy-1-methoxy-6a,7-dehydroaporphine (**28**, 2.9 mg), lysicamine (3.0 mg), D,L-armepavine (**29**, 27.4 mg), and pronuciferine (8.3 mg) were obtained (Nakamura et al., 2013).



7.2.4. Sida rhombifolia, Sida spinosa and Sida cordifolia (Malvaceae)

All three *Sida* species are worldwide weeds (including India; Holm et al., 1979, p.: 335-356). In Hindi *Sida* species are called 'bariara', 'kareta', 'bhundli', 'lal berela' and in Sanskrit 'sahadêvâ', 'viśvadêvâ', 'rishyaprôktâ', 'nâgabalâ', 'balâ' (Rajan and Sethuraman, 2008; Hoernle, 2011). The roots of *Sida cordifolia* contain the β-phenylethylamine type alkaloids PEA (**1**) ephedrine (**30**), pseudoephedrine, the carboxylated tryptamines hypaphorine (**8**) and *S*-(+)-N_b-methyltryptophan methyl ester (**31**) and the quinazoline alkaloids vasicine (peganin, **32**), vasicinol (**33**) and vasicinone (**34**, Ghosal et al., 1975). The same substances are reported from the roots and aerial parts of *Sida spinosa* and *Sida rhombifolia*, with the exception of methyltryptophan methyl ester and the additional presence of hypaphorine methyl ester in *Sida spinosa* and that, while the aerial parts of *Sida rhombifolia* seem to lack carboxylated tryptamines, they additionally contain *N*-methyl-β-phenethylamine (**35**, Prakash et al., 1981). Chaves et al. (2013) furthermore report the presence of the indoquinoline alkaloids cryptolepine (**36**) and cryptolepinone (**37**) in the aerial parts of *Sida rhombifolia*.

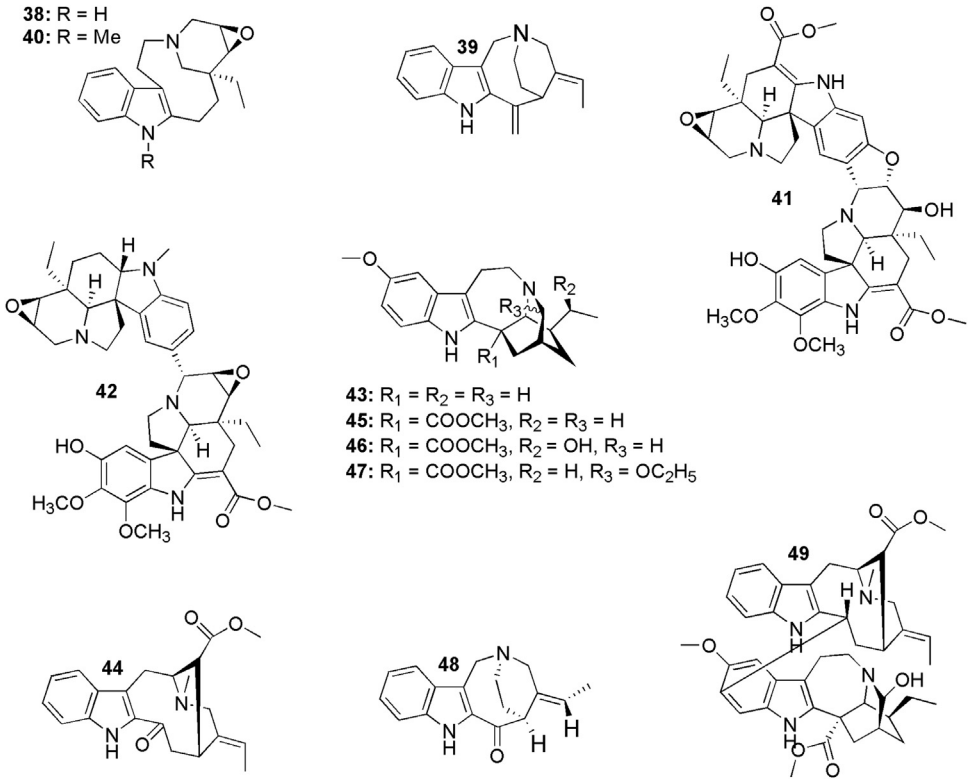
From 3.5 kg dried roots of *Sida cordifolia* Ghosal et al. (1975) obtained PEA (42 mg), ephedrine (22 mg), +-ephedrine (13 mg), plus a 22 mg mixture of ephedrine and +-ephedrine, vasicinone (126 mg), vasicine (37 mg), vasicinol (31 mg), choline (76 mg), hypaphorine (14 mg), and betaine (84 mg). Quantitative extraction of the alkaloid content of 5 kg dried aerial parts of *S. rhombifolia* by Prakash et al. (1981) afforded PEA (470 mg), *N*-methyl-β-phenylethylamine (190 mg), ephedrine (136 mg), +- ephedrine (98 mg), vasicinol (12 mg), vasicinone (36 mg), vasicine (32 mg) choline (85 mg) and betaine (93 mg).



7.2.5. Tabernaemontana divaricata (Apocynaceae)

Tabernaemontana divaricata is a widespread latex bearing garden plant, rich in indole alkaloids from the vincosan, aspidospermatan, plumeran, bis-indole and ibogan group (Pratchayasakul et al., 2008). In Hindi the species is referred to as 'cadni' and in Sanskrit 'nata' or 'nandivrksah' (Sala, 2010, p.: 232; Hoernle, 2011). Kam et al. (2003) isolated 23 alkaloids with an overall yield of 1068 mg kg^{-1} from the leaves of the double flower variety of *Tabernaemontana divaricata*. Alkaloids affording the highest yields were voaphylline (**38**, 260 mg),

apparicine (**39**, 220 mg), *N*(1)-methylvoaphylline (**40**, 120 mg), conophylline (**41**, 116 mg) and conofoline (**42**, 105 mg), while only 2 mg ibogaine (**43**) was obtained (Kam et al., 2003). From the stem-bark of the same *Tabernaemontana divaricata* variety Kam et al., (2004) characterised 42 alkaloids with an overall yield of 647.7 mg kg^{-1}. The highest yields were obtained for vobasine (**44**, 97 mg) voacangine (**45**, 91 mg), voacristine (**46**, 58 mg), (3*R*/3*S*)-3-ethoxyvoacangine (**47**, 56 mg) but only 2.4 mg ibogaine was obtained. Kam et al. (2004) for the first time isolated conolidine (**48**, 1.3 mg/kg) a C5-nor stemmadenine, which was found to exert promising analgesic activity in mice (Tarselli et al., 2011). Chaiyana et al. (2013) estimated the content of the bis-indole alkaloid 3'-*R*/*S*-hydroxyvoacamine (**49**) obtained from 3.36 kg *Tabernaemontana divaricata* stem at 3390 mg. Bao et al. (2013) obtained 42 grams of alkaloidal fraction and isolated the psychoactive ibogaine (50 mg), several voacangine derivatives and a number of other ibogaine type alkaloids from 5 kg dried *T. divaricata* stem.



7.2.6. Tinospora cordifolia (Menispermaceae)

Tinospora cordifolia is a deciduous twiner with heart shaped leaves occurring from Kumaon (Uttarakhand), Jammu and Kashmir state in the north to the extreme south of India (Williamson, 2002, p.: 302; Kumari et al., 2013). The colour of the succulent stems varies from a creamy greenish brown to yellowish brown (Fig. 2). It is reported that freshly cut stems immediately assume a yellow colour when exposed to air (Neeraja and Margaret, 2013). Holm et al. (1979, p.: 363) list the species as a weed for India. The species is called 'gudûchî', 'guluchi' or 'amritâ' in Sanskrit and 'gulancha', 'guruchi', 'giloy' or 'amrita' in Hindi (Bisset and Nwaiwu, 1983; Williamson, 2002; Sala, 2010, p.: 283; Hoernle, 2011). From *Tinospora cordifolia*, which is called 'Amrita', both in the BM and Ayurvedic herbal medicine, Phan et al.

Fig. 2. *Tinospora cordifolia–foto* taken in Kathmandu, Nepal, March 2009 and courtesy of Todd Caldecott.

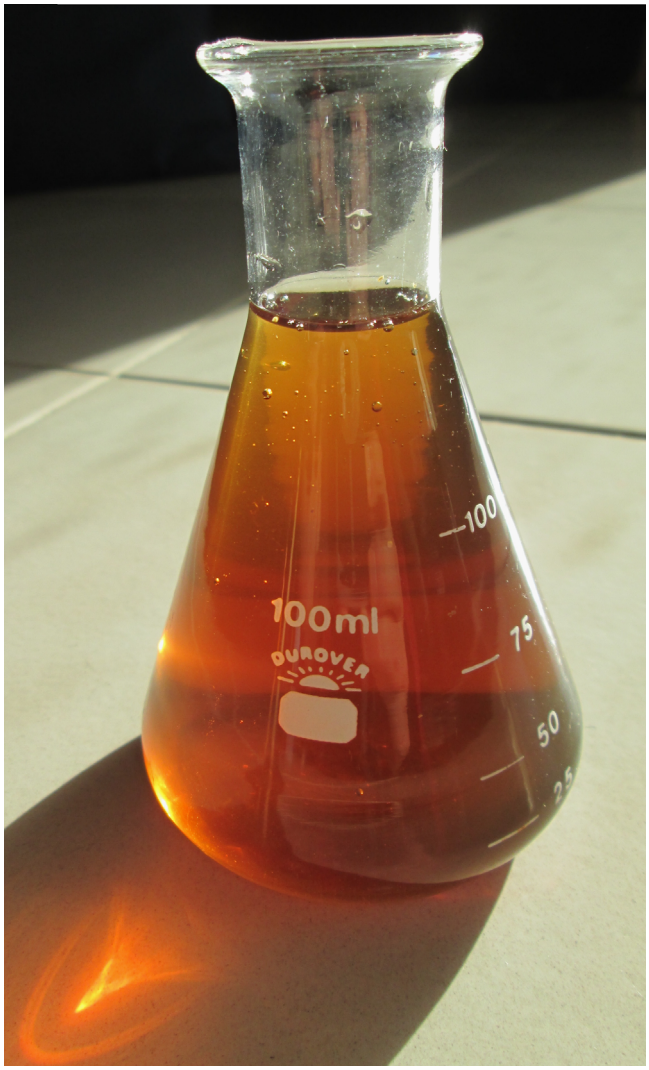
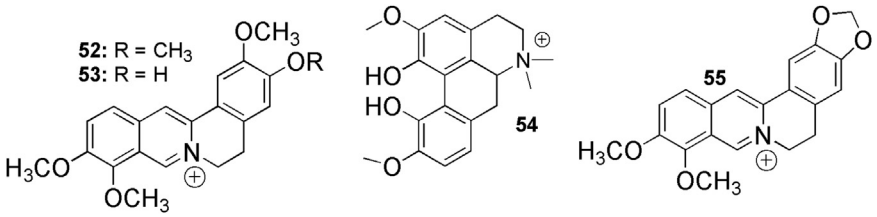


Fig. 3. *Tinospora cordifolia* stem powder extracted with baking soda ($NaHCO_3$) and water.

(2010) report the isolation and identification of two aporphine glycosides, *N*-formylasimilobine-2-O-*β*-D-glucopyranosyl-(1→2)-*β*-D-glucopyranoside (**50**, 28 mg) and *N*-acetylasimilobine-2-O-*β*-D-glucopyranosyl-(1→2)-*β*-D-glucopyranoside (**51**, 2.5 mg) from 2 kg aerial parts. From 920 g powdered *Tinospora cordifolia* stem Patel and Mishra (2011) obtained 28 g extract and from a 15 g aliquot thereof isolated the two protoberberine bases palmatine (**52**, 2467 mg) and jatrorrhizine (**53**, 748 mg) as well as 140 mg of the aporphine alkaloid magnoflorine (**54**). Srinivasan et al. (2008) furthermore estimate the berberine (**55**) concentration based on a HPLC method at around 0.3% of dried plant material. Extrapolated on the hypothetical extraction of 1 kg *Tinospora cordifolia* stem, around 1500 mg jatrorrhizine, 4900 mg palmatine and 3000 mg berberine could potentially be obtained. Palmatine has a yellow colour, jatrorrhizine is reddish-brown and berberine has an intense yellow colour and is therefore also used to dye textiles (Römpp-Lexikon, Regitz, 1997, p.: 520). We have extracted *Tinospora. cordifolia* stem powder obtained from online sources with water and baking soda (sodium bicarbonate, $NaHCO_3$) receiving an amber or honey coloured golden shining extract (Fig. 3).



8. Discussion

Flattery and Schwartz suggested that the Syrian rue (*Peganum harmala*) corresponds to Haoma as well as Soma. *P. harmala*, is a drought tolerant species today distributed around the Mediterranean basin extending east to the northern part of India and listed as a weed for

Turkey and Afghanistan (Holm et al., 1979). Flattery and Schwartz (1989), however, also acknowledge that *Peganum harmala* seems to have become established in India only more recently being introduced by Muslim societies, since the local names used in India derive directly from either the Arabic (harmel) or Persian (isfan; p.: 42). The fact that *Peganum harmala* has not been identified throughout the BM by Hoernle (2011) does lend additional support to the concerns raised by Flattery and Schwartz. With respect to the theory that Soma was nothing else but an *Ephedra* sp., Falk (1989) does not ignore that on the Indian subcontinent *Ephedra* spp. grow only in the northern and mountainous regions of Afghanistan, Pakistan and India at altitudes between 1200 and 4000 m a.s.l. *Ephedra* species would thus have had to be traded ("Soma-buyer") if they played a role in the Vedic Soma ritual (Falk, 1989). McDonald (2004) on the other hand acknowledges, that the hypothesis, that lotus as a single species would be the equivalent of soma, lacks a chemical and pharmacological analysis and verification.

No such biogeographic doubts and far less phytochemical uncertainties exist with the species presented in the results section and contained in the Amrita recipes of the BM. All eight species are common throughout India. Altogether, the chemistry of these eight species (*D. gangeticum*, *M. pruriens*, *N. nucifera*, *Sida cordifolia, Sida rhombifolia, Sida. spinosa*, *T. cordifolia* and *T. divaricata*) includes several notorious and potential psychoactive and psychedelic substances, and alkaloid classes, namely tryptamines, phenylethylamine, ephedrine, aporphine alkaloids, ibogaine, and L-DOPA. Moreover, MAO and AChE interfering protoberberine alkaloids as well as potentially neurotoxic tetrahydroisoquinolines and β-carbolines are present. The presence of aporphine alkaloids and the asimilobine moiety in both ingredients of the Amrita oil, *N. nucifera* as well as *Tinospora cordifolia*, is intriguing. The phytochemical profile and associated pharmacology of *Nelumbo nucifera* renders McDonald's (2004) hypothesis, that *Nelumbo nucifera* corresponds directly to Soma, not very plausible, however. By adding small amounts of the amphoteric sodium bicarbonate to the watery maceration of *Tinospora cordifolia* stem powder we obtained a stronger gold-brown colouring than extracting with pure water, but the relevance to the present discussion is not yet clear. We are aware that for many other species mentioned in these Amrita recipes no or only scarce phytochemical and pharmacological data exist and that ongoing research efforts may help to identify more species with potential psychoactive properties.

8.1. Serotoninergic, dopaminergic and adrenergic interactions

Upon oral ingestion the hallucinogenic tryptamines (5-MeO-DMT, 5-OH-DMT, DMT and tryptamine) as well as the psychoactive PEA are readily catabolized by MAO. Tryptamines are mainly deaminated by MAO-A (Shen et al., 2010) and in occasions when MAO-A is deactivated they may also be catabolized by the B isoform (Nagatsu, 2004). PEA is predominantly catabolized by the B subtype (Buckholtz and Boggan, 1977). The potent psychedelic 5-MeO-DMT is either deaminated by MAO-A or *O*-demethylated by cytochrome P450 2D6 resulting in the even more active 5-OH-DMT (bufotenine), which is finally deaminated by MAO (Shen et al., 2010). 5-OH-DMT is about three-times more potent towards the serotonin (5-HT) receptor (affinity: 5-HT_{2A} > 5-HT_{1A}) than 5-MeO-DMT (affinity: 5-HT_{1A} > 5-HT_{2A}), which is up to 10 times more potent than DMT in humans (Shen et al., 2010).

1-Me-tetrahydrobetacarboline (1-Me-THBC), was shown to inhibit ^{3}H-5-HT (tritiated serotonin) and ^{3}H-DA (tritiated dopamine) uptake by human platelets with IC_{50} values of 6.4 and 1.0 μM respectively (Airaksinen et al., 1980). Moreover, Komulainen et al. (1980) have shown that 1-Me-THBC inhibits 5-HT uptake by rat synaptosomes (IC_{50} = 12 μM), the DA uptake into striatal synaptosomes (IC_{50}=70 μM) as well as noradrenaline (NA) uptake by cortical rat synaptosomes (IC_{50}=92 μM). Similar to these *in vitro* data assessed for 1-Me-THBC, 1,2-Me-THBC (**10**) present in *D. gangeticum* might lead to elevated inter-synaptical 5-HT, DA and NA concentration in human brain tissues.

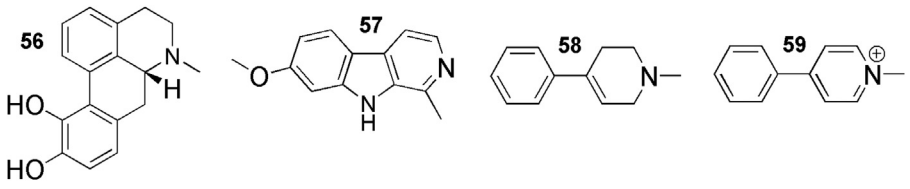
Nornuciferine obtained from *Nelumbo nucifera* and asimilobine, present in *Nelumbo nucifera* and in its glucosylated *N*-formyl and *N*-acetyl form also in *Tinospora cordifolia*, have been shown to interact agonistically with the 5-HT_{1A} receptor *in vitro* with K_i values of 10 and 20 μM, respectively (Hasrat et al., 1997). Also the bisbenzylisoquinoline neferine isolated from the seeds and leaves of *Nelumbo nucifera* (Kashiwada et al., 2005; Sugimoto et al., 2010) was shown to exert antidepressant-like effects in mice mediated via the 5-HT_{1A} receptor (Sugimoto et al., 2010). Shoji et al. (1987), however, report 5-HT antagonistic properties for asimilobine as well as lirinidine. Apomorphine (**56**), used as an agent in the treatment of Parkinson's Disease (PD) and closely related to magnoflorine found in *Tinospora cordifolia* as well as nuciferine, asimilobine and lysicamine obtained from *Nelumbo nucifera*, shows considerable affinities towards different subtypes of dopamine, serotonine and adrenergic receptors (Millan et al., 2002).

Berberine and palmatine, both present in *Tinospora cordifolia* were found to interact with the 5-HT_2 receptor, displacing the radioligand with an IC_{50} of 1.9 and 2.9 μM, respectively (Schmeller et al., 1997). It remains, however, unclear what kind of effect berberine and palmatine mediate through 5-HT_2 receptor interaction. Berberine and palmatine also bind to alpha$_1$- and alpha$_2$-adrenergic receptors displacing bound radioligands with an IC_{50} of 3.2 and 0.476 μM (berberine) and 5.8 and 0.956 μM (palmatine) probably transmitting antagonistic effects (Schmeller et al., 1997).

Ephedrine, present in *Sida* spp., apart from releasing noradrenaline, leads to increased extracellular dopamine concentrations in brain tissues including the striatum and the substantia nigra (Bowyer et al., 2000; Munhall and Johnson, 2006).

The pharmacologic interactions of ibogaine and ibogaine type alkaloids present in *Tabernaemontana divaricata* within the CNS are multiple and therefore particularly complex. Low micro molar affinities of ibogaine with the serotonergic, nicotinic, *N*-methyl-D-aspartate, μ and κ opioid system, sigma receptors as well as sodium channels have been detected (Alper, 2001).

Excessive intake of L-DOPA through *Mucuna pruriens* seeds has been associated with toxic psychosis and peripheral side effects such as palpitations and headache (Infante et al., 1990; Mahajani et al., 1996) and can therefore not be considered to contribute to an acceptable psychedelic effect. Such as the Amrita-oil was indicated against the 80 nervous diseases, *Mucuna pruriens* seeds are still used in Ayurvedic medicine for the treatment of PD and murine data indicates that L-DOPA containing *Mucuna pruriens* seed extract is more effective than an equivalent dose of L-DOPA, suggesting synergistic effects (Kasture et al., 2009).



8.2. Monoamine oxidase inhibition

Jatrorrhizine was shown to inhibit both, MAO-A and B obtained from rat brain using 5-HT and PEA as a substrate in a non-competitive manner with IC_{50} values of 4 and 62 μM, respectively, while berberine inhibited MAO-A with an IC_{50} of 126 μM (Kong et al., 2001). Castillo et al. (2005) assessed with two independent *in vitro* assays that berberine also inhibits MAO-B obtained from mouse liver mitochondria with IC_{50} values of 89 μM (benzylamine as substrate) and 90 μM (fluorescence method). Lee et al. (1999) measured the IC_{50} of plamatine with mouse brain MAO and kynuramine as substrate at 90.6 μM, but Kong et al. (2001) found no inhibitory activity of plamatine up to a concentration of 200 μM. Due to the slightly conflicting results and divers assay conditions a standardized assessment of the MAO-I properties of these protoberberine isoquinolines could provide clarifications. No pharmacologic data are available for 2-methyl-tetrahydroharman (1,2-dimethyl-1,2,3,4-tetrahydro-β-carboline, **10**) but the closely related tetrahydroharman (1-methyl-1,2,3,4-tetrahydro-β-carboline) has been found to moderately inhibit (EC_{50} = 120 μM) mouse brain MAO with tryptamine as a substrate (Buckholtz and Boggan, 1977).

Bembenek et al. (1990) as well as Thull et al. (1995) report on the inhibitory activity of a range of isoquinoline derivatives including 1,2,3,4-tetrahydroisoquinolines (TIQ) and *N*-methyl-TIQ on MAO-A and B. Bembenek et al. (1990) identified the *N*-methylated TIQ as an inhibitor of human MAO-A with a K_i value of 27 μM. Inhibitory values (IC_{50}) found by Thull et al. (1995) range from 1 to 130 μM for the A subtype and from 10 to 270 μM for the B subtype. The most potent MAO-B inhibitors were 1,2,3,4-tetrahydroisoquinoline and 2-methyl-1,2,3,4-tetrahydroisoquinoline with K_i's of 15 and 1 μM, respectively (Thull et al., 1995).

8.3. Acetylcholine and butyrylcholine metabolism interactions

Berberine binds, probably mediating agonistic effects, to the muscarinic (mAChR) and nicotinic acetylcholine receptors (nAChR) displacing bound radioligands with an IC_{50} of 1 and 35.5 μM, while palmatine interacts only with the mAChR with an IC_{50} of 4.1 μM. At the same time both alkaloids inhibit acetyl- and butyrylcholine esterase with an IC_{50} of 167.4 and 55.8 μM (berberine) and 124.5 and 425.6 μM (palmatine; Schmeller et al., 1997).

The benzyltetrahydroisoquinolines coclaurine, *N*-methylcoclaurine, and armepavine present in *N. nucifera* were shown to inhibit different cloned human nACh receptor subtypes with IC_{50} values in the range of 132 – > 500 μM (coclaurine), 23 – > 500 μM (*N*-methylcoclaurine) and 14–18 μM (armepavine), and IC_{50} values for the functional affinity of 18 – > 200 μM (coclaurine), 4.8–25 μM (armepavine; Exley et al., 2005).

Moreover, 3′-*R*/*S*-hydroxyvoacamine from *Tabernaemontana divaricata* was found to non-competitively inhibit acetylcholine esterase with an IC_{50} value of 7.00 μM (Chaiyana et al., 2013).

8.4. The MAO-I 'Ayahuasca-hypothesis'

Ott (1997) reports his subjective threshold-level for the perception of a psychedelic effect with harmine (**57**) and DMT (**6**) to be 1.5 mg/kg harmine (120 mg/80 kg body weight) combined with 30 mg DMT (0.375 mg/kg; see also Callaway, 1999). Callaway (1993) states that a 0.5–1 mg/kg oral dose of harmine combined with 0.5 mg/kg DMT or 0.1 mg/kg 5-MeO-DMT (**7**) is also effective. Hence, there seems to be some range of tolerance in the dosage of the two components since it appears that more MAO substrate can compensate for lower MAO-I concentration. The MAO-I activity of harmine has been assessed *in vitro* with mouse brain MAO and tryptamine as a substrate at an EC_{50} of 0.08 μM (Buckholtz and Boggan, 1977). Compared to the *in vitro* MAO-A inhibition of jatrorrhizine (**53**, IC_{50}=4 μM) assessed with rat brain MAO and serotonin as a substrate (Kong et al., 2001), harmine shows 50 times higher potency. However, harmine selectively inhibits MAO-A (Gerardy, 1994), while jatrorrhizine, berberine (**55**) and eventually also palmatine (**52**) concomitantly inhibit MAO-B (Lee et al., 1999; Kong et al., 2001; Castillo et al., 2005). Therefore, synergistic MAO-I effects can be expected by a protoberberine-rich *Tinospora cordifolia* extract.

Taking into account, both the qualitative as well as the quantitative phytochemical profile of the discussed species we argue that a psychoactive potion could most probably be obtained by mixing a concentrated MAO-I juice of *Tinospora cordifolia* with either a *Desmodium gangeticum* and/or a *Sida* sp. extract, eventually as described in the 9th Mandala and the BM, previously brought into an oily form. We propose that *Tinospora cordifolia* in high doses blended with *Desmodium gangeticum* potentially leads to colourful psychedelic visions, while *Tinospora cordifolia* blended with *Sida* spp. would induce exhilarating amphetamine-like sensations. Also *Nelumbo nucifera* and *Tabernaemontana divaricata* have the potential to add to the overall psychoactivity of a multi-extract combination.

8.5. Toxicity

Tetrahydro-β-carbolines (THβC) and tetrahydroisoquinolines (TIQ) are considered potential endogenous and exogenous neurotoxins relevant in the aetiology of PD (Nagatsu, 1997). Especially the *N*-methylated TIQ of *Nelumbo nucifera* (**18** and **29**) as well as the 1,2-dimethylated THβC (**10**) and the *N*-methylated β-carbolinium cation (**9**) of *Desmodium. gangeticum* are of toxicological concern. *N*-Methylated THβC and *N*-methylated TIQ are structural analogues of 1-methyl-4-phenyl-1,2,3,6-tetrahydropyridine (MPTP, **58**), a precursor, which upon catalyzation by MAO-B within non-dopaminergic cells converts to MPP^+ (**59**), a PD inducing neurotoxin (Przedborski et al., 2000). The high affinity of MPP^+ towards the plasma membrane dopamine transporter permits a selective accumulation of MPP^+ in dopaminergic cells (Przedborski et al., 2000). Once inside dopaminergic cells, MPP^+ inhibits mitochondrial activity, which leads to a degeneration of the dopaminergic neurons in the substantia nigra (Fields et al., 1992; Neafsey et al., 1995; Nagatsu, 1997). Endogenously or environmentally derived β-carbolines and TIQ oxidised by haem peroxidases or MAO (Naoi et al., 1989a; Herraiz et al., 2007) and bio-activated by *N*-methyltransferases (Naoi et al., 1989b; Gearhart et al., 2000) are therefore being discussed as possible pro-toxins in the aetiology of PD (Nagatsu, 1997). In the cerebro-spinal fluid of deceased Parkinson patients elevated levels of *N*-methyl-β-carbolinium cations have been found (Matsubara et al., 1993; 1995). Moreover, subcutaneous administration of 22 mg/kg 1-benzyl-1,2,3,4-tetrahydroisoquinoline daily over 66 days to a subject of *Macaca fasciularis* led to the appearance of symptoms typical for PD (Kotake et al., 1996). Remarkably, the *N*-methylated-β-carbolinium (**9**) present in *Desmodium. gangeticum* does not need to be activated

by MAO-B or methyltransferase because it presents the structural features of a neurotoxin already. Also, upon oxidation by MAO the *N*-methylated TIQ may readily become MPP^+ analogues.

Amphetamine-like compounds are potentiated by MAO-I, which can trigger hypertensive crisis including symptoms such as headache, sweating, pallor, nausea, vomiting and fright (DeKorne et al., 2002, p.: 18). When experimenting with MAO-I one should take dietary precautions and avoid ingesting food with high amine content such as "cheese, especially aged cheese, beer, wine pickled herrings, snails, chicken livers, yeast products, figs, raisins, pickles, sauerkraut, coffee, chocolate, soy sauce, cream or yogurt" (DeKorne et al., 2002, p.: 18).

9. Conclusions

The multidisciplinary analysis of two Amrita recipes recorded during the 6th century A.D. in the Bower Manuscript and advertised amongst others as panaceas and as a remedy to cure nervous diseases revealed several plant species containing CNS interacting and psychoactive alkaloids. We argue that these recipes are related to the Rigvedic Soma since they are called 'Amrita' (non-death), a synonym for 'Soma', and referred to as 'Ambrosia' (food of the gods). All identified and discussed alkaloid-rich species (*Tinospora cordifolia, Sida* spp., *Mucuna pruriens*, *Nelumbo nucifera*, *Desmodium gangeticum*, *Tabernaemontana divaricata*) are widely used medicinal herbs with an important role in Ayurvedic, Chinese and Thai Medicine. We suggest that the Rigvedic Soma was a mixture of a watery, protoberberine alkaloid-rich *Tinospora cordifolia* extract with MAO-I properties and a tryptamine-rich *Desmodium gangeticum* and/or an ephedrine and PEA containing *Sida* spp. extract. *Tinospora cordifolia* mixed with *Desmodium gangeticum* might provide a psychedelic experience with visual effects, while a combination of *Tinospora cordifolia* with a *Sida* spp. extract might lead to more euphoric and amphetamine-like experiences. Although the reviewed phytochemical analyses were not strictly quantitative, the alkaloid yields, especially for *Tinospora cordifolia*, which is still called Amrita today, as well as for *Desmodium gangeticum*, are considerable. Under acidic conditions alkaloids are generally water-soluble and under neutral and basic conditions liposoluble. With curdled milk, water and plant oils as reported in the description of the Soma preparation of the 9th Mandala, the ancient Indo-Aryans were in possession of the means to extract the pharmacologically relevant compounds. We can, however, not exclude that among the herbal ingredients mentioned in the Amrita recipes other species with psychoactive secondary metabolites are present than the ones we have identified. Only an experimental *in vivo* study can clarify what kind of pharmacologic effects on the human psyche a mixture of extracts made from *Tinospora cordifolia*, *Desmodium gangeticum* and *Sida* spp. has. The same accounts for the overall Amrita recipes described in the Bower Manuscript. Although synergistic effects of such a mixture can be anticipated, for the induction of a psychoactive effect elevated doses of the different ingredients would be required. Considering the structural features of the chemical compounds present in these species, concerns regarding the neurotoxicity of a highly concentrated potion are appropriate.

"And if anything should go wrong, there's soma. Which you go and chuck out of the window in the name of liberty, Mr. Savage. Liberty! He laughed." (Brave New World, Aldous Huxley, 1932).

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