# "Ayahuasca-like" effects obtained with Italian plants

by *Francesco Festi* & *Giorgio Samorini* .

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The authors present the results of investigation carried out in the *ayahuasca* analogues research field (*pharmahuasca*), using a species of *Phalaris* (*Gramineae*) native to or naturalized in Italy as source of tryptamine alkaloids. As a source of ß-carboline alkaloids, the seeds of *Peganum harmala* (*Zygophyllaceae*), a plant living in Mediterranean countries including Italy, have been used. As a result of some autoexperiments aimed at reproducing a kind of 'ayahuasca effect', the mixing of the acqueous extracts of young leaves of *Phalaris aquatica* L. and seeds of *P.harmala* proved to be strongly psychoactive; this further confirms the validity of the model of the action of alkaloids contained in the *ayahuasca* potions, which is the basis of the principles of *pharmahuasca*.
With regard to the quantities of psychoactive indolic alkaloids in *P.aquatica* and *P.arundinacea*, great deal of literature exists in the agronomic and veterinary fields. Genetic, environmental, physiological and cultural factors which may significantly influence the concentration of these alkaloids are discussed. Lastly, the results of a series of chemical analysis carried out on the main European species of the *Phalaris* genus will be referred to, up to now unexplored from the point of view of its psychoactive indolic alkaloid content.

**'Efecto ayahuasca' obtenido con plantas italianas.**
Los Autores presentan los resultados des indagaciones en el campo de investigación de los análogos del *ayahuasca* (*pharmahuasca*), utilizando, como fuente de alcaloides triptamínicos, algunas especies de *Phalaris* (Gramineae) originarias o naturalizadas en Italia. Como fuente de alcaloides ß-carbolinicos, fueron utilizadas las semillas de *Peganum harmala* (Zygophyllaceae), una planta que vive en los países del Méditerraneo, incluida Italia. Como consecuencia de algunas autoexperimentaciones, con el propósito de reproducir una especie de 'efecto ayahuasca', la combinación de extractos acuosos de hojas jovenes de *Phalaris aquatica* L. y de semillas de *P.harmala* resultó fuertemente psicoactiva; esto confirma una vez más la validez del modelo de acción de los alcaloides contenidos en las bebidas de *ayahuasca*, y que es la base de los principios de la *pharmahuasca*.
En lo que se refiere al contenido de alcaloides indolicos psicoáctivos en *P.aquatica* y *P.arundinacea*, existe una vasta literatura en los sectores agronomico y veterinario, siendo estas especies ampliamente utilizadas como forrajes en varias regiones del mundo. Se discuten los factores genéticos, ambientales, fisiológicos y culturales, que pueden influenciar significativamente las concentraciones de estos alcaloides. Finalmente, se presentan resultados de una serie de análisis químicas realizadas en las principales especies europeas del género *Phalaris*, aún no exploradas en sus contenidos de alcaloides indolicos psicoáctivos.

The psychoactive alkaloids found in the genus *Phalaris*, particularly N,N-dimethyltryptamine (DMT) and 5-methoxy-N,N-dimethyltryptamine (5-MeO-DMT), are known to be the entheogenic agents in the Amazonian drink *ayahuasca*. In this widely used potion the inhibitory action on the monoamine oxidase by the ß-carbolines (particularly harmine, its main component) is essential to make the indolakylamines orally active, otherwise effective only parenterally [McKenna, 1992; McKenna & Towers, 1984; McKenna *et al.*, 1984; Ott, 1993; 1994a; 1994b; Rivier & Lindgren, 1972]. Already few years after the proposal about the interaction between DMT and ß-carbolines as *ayahuasca* mechanism of action, there were sporadic attempts to reproduce this effect by using the only active agents or plants other than the Amazonian ones [Ott, 1994a; 1994b]. We must mention the pioneer work of Jeremy Bigwood [1978 in Ott, 1994a], who ingested an *ayahuasca*-like preparation constituted by harmine and DMT, obtaining an action comparable to that of the original *ayahuasca*. Also the "underground" publications by "Gracie & Zarkov" [1985; 1986] are very important; they combined DMT with enriched alkaloids extract of *Peganum harmala* L., a Zygophyllaceous plant containing a valuable amount of harmine and other ß-carboline alkaloids. The outcomes of these experiments were reported to be clearly entheogenic, with a threshold of about 20 mg of DMT combined with 5 g of *Peganum harmala* seeds. More recently, an increasing attention has been paid to *pharmahuasca* or *Ayahuasca borealis* - as these preparations, reproducing the "*ayahuasca*-like effect" with chemical substances and plants other than those originally used in Amazonia, have been called.

In this context, the experiments carried out by Jonathan Ott and recently published are very interesting. The author reports about the ingestion of varying amounts of *Peganum harmala* seeds

* Società Italiana per lo Studio degli Stati di Coscienza - Italian Society for the Study of the States of Consciousness. Museo Civico di Rovereto - Via Calcinari 18 - I-38068 ROVERETO (TN) Italy

extract together with pure indoalkylamines or extracts of *Psychotria viridis* RUIZ & PAVON (*Rubiaceae*), *Desmanthus illinoensis* (MICHAUX) MACM. (*Leguminosae*) or *Acacia phlebophylla* F. VON MÜLLER (*Leguminosae*). 4 g of *Peganum* seeds and an equivalent amount of 30 mg of DMT are reported to be clearly psychoactive; the same results can be achieved by using MAO inhibitors contained in pharmaceutical preparations [OTT, 1993; 1994a; 1994b]. Parallel experiments also proved the possibility of reproducing the "*ayahuasca*-like effect" with MAO inhibitors in combination with 5-MeO-DMT [CALLAWAY, 1993; CALLAWAY, 1992 in OTT, 1994a; LEUNER & SCHLICHTUNGEN, 1989] and DET [OTT, 1994a].

The "psychonautic" exploration of the genus *Phalaris* as a source of indolalkylamines in the *Ayahuasca borealis* has a shorter history, up to now tied to the "underground" circle. The *Entheogen Review* published in 1992 a note, written under the pseudonym of "John Appleseed" describing a simple method to extract the alkaloids from *Peganum harmala* and other plants [APPLESEED, 1992; 1993a; 1993b]. At the end of the next year the review claimed the full entheogenic activity of *Phalaris arundinacea* (var. "Turkey Red" and "Yugoslavian Fresh Cut") extract smoked with inert matter [DEKORNE, 1993b; 1994a; 1994c]. At the same time, positive outcomes were reported, referred to some experiments with the ingestion of *Peganum* extract (125 mg) and *Phalaris arundinacea* var. "Turkey Red" extract (30-50 mg) [APPLESEED, 1993a; 1993b; DEKORNE, 1993a; 1993b; 1994a; 1994b; 1994c]. .

In the present work we are communicating some results of the researches that we have been carrying out about the genus *Phalaris*, including some auto-experiments of *pharmahuasca* obtained with an Italian strain of *Phalaris aquatica*.

## Botany and chemistry of the genus *Phalaris* L.

The genus *Phalaris*, belonging to the family *Graminaceae* (also called *Poaceae* or *Gramineae*), includes, according to the most recent revisions, about 15 to 20 species (depending on the concept of species adopted by the authors) [ANDERSON, 1961; BALDINI, 1993; PRAT, 1960]. Some specific or subspecific entities are widespread in the temperate and subtropical areas of both hemispheres; however, the determination of the natural distribution of the genus is difficult, since many species have been introduced in some parts of the world as forage or ornamental plants [HITCHCOCK, 1950; VOSE, 1959; HEATH & HUGHES, 1961; TUTIN in TUTIN et al., 1980; GÖHL, 1982; WALTERS et al., 1984; MARTEN, 1985; WASSON & DALLWITZ, 1992]. Undoubtedly, the Mediterranean and Macaronesian phytogeographical regions have the maximum of taxonomic variability and can be considered as the differentiation centre for the genus. In fact, at least 13 entities are known in Europe [BALDINI, 1993; MEUSEL et al., 1965; TUTIN in TUTIN et al., 1980; WALTERS et al., 1984]:

- *P. arundinacea* L., sometimes segregated from the genus *Phalaris* as *Typhoides* MOENCH, *Digraphis* TRIN., *Baldingera* DUMORT. or *Phalaroides* RAUSCH. It is widespread in wet places, particularly on the riversides and along the canals, also outside the strictly Mediterranean region and almost in every state of the European continent. Besides the type, the variety *picta* L. is also cultivated as an ornamental plant: it differs from the variety *arundinacea* through the white or yellowish stripped leaves.
- *P. caesia* NEES is very similar to the above mentioned species, also having non-winged keels of the glumes and panicle lobate at maturity. It occurs in South-western Europe (Portugal, Spain and Southern France) as well as in tropical and Southern Africa.
- *P. rotgesii* (HUSNOT) BALDINI is also similar to *P. arundinacea*, of which it is considered a variety by some authors. It has a very restricted distribution, occurring only in Corsica and Sardinia.
- *P. aquatica* L. (= *P. nodosa* MURRAY; *P. tuberosa* L.; *P. bulbosa* Auct. non L.; *P. commutata* ROEM. & SCHULT.) is naturally widespread in the Mediterranean areas of Europe. It is also widely introduced as forage in many parts of the globe, where it is often adventive or naturalized.
- *P. stenoptera* HACK. is sometimes treated as an infraspecific taxa of *P. aquatica*, of wich it may constitute a modified form. It probably originated in Northern Africa (Morocco) but it is present, adventive or naturalized, also in many parts of Europe, Australia and America, because of its use as forage.
- P. *truncata* GUSS. ex BERTOL., comes from the Mediterranean region. It has been used as animal food very rarely and only around the Mediterranean basin.
- *P. canariensis* L. Most authors think it originally came from the Canary Islands and North-western Africa. However, it is widely cultivated as an ornamental plant or for the seeds (as bird food) and so it is present almost everywhere in Europe with adventive or naturalized status. This

wide, but probably secondary distribution, has led some authors (such as BALDINI [1993]) to think that the species originally came from some areas of the Mediterranean region.

- *P. minor* RETZ. grows wildly in most European countries on the Mediterranean Sea. It is sometimes found casual or naturalized, owing to its growing as forage or, not frequently, as an ornamental plant.
- *P. brachystachys* LINK in SCHRADER grows in the Mediterranean and Macaronesian regions, where it has sometimes been used as fodder. It is therefore found also casual, but very rarely outside its natural distribution area.
- *P. paradoxa* L. has, more or less, the same distribution area as the above mentioned species. It is seldom grown as ornamental.
- *P. coerulescens* DESF. is also distributed in the Mediterranean and Macaronesian regions, where it seems to have little or no economical value.
- *P. maderensis* (MENEZ) MENEZ has a very restricted distribution, being known only from Madeira and the Canary Islands.
- *P. hirtiglumis* (TRABUT) BALDINI (=*P. bulbosa* L. *var. hirtiglumis* TRABUT) comes originally from North Africa but recently has been reported also in Italy and Southern France.

Most of the above-mentioned species have been used as forage, sometimes also with satisfactory results and promising developing prospects. However, *P. arundinacea* and *P. aquatica* are the species most widely utilized for such a purpose, owing to their good agronomical features [BERG, 1978; HEATH & HUGHES, 1961; MARTEN, 1985; VOSE, 1959]. The first one has been cultivated in Europe since 1749 and in America since 1885; nowadays its growing is particularly widespread in the temperate areas of the American continent and Australia, both in the pastures and for the control of grassed waterways or stream banks, because of its fast growth it prevents soil erosion. As a matter of fact just the U.S.A. and Canada are presently the most important seed producers in the world and in these countries more than 20 cultivars have been selected [*ibid.*]. On the contrary, the cultivation area of *P. aquatica* emphasizes its adaptation to the rainy mediterranean/subtropical climates. In fact, apart from its native countries, it is also widely used as a forage in Australia, North- and South-Africa, in the Southern states of the U.S.A. and in South-America [BALTENSBERGER & KALTON, 1958; 1959; HEATH & HUGHES, 1961; HITCHCOCK, 1950; HOVELAND & ANTHONY, 1971; MARTEN, 1985; VOSE, 1959].

Already during the first years of the intensive utilization [GALLAGHER *et al.*, 1966a; LEE & KUCHEL, 1953; LEE *et al.*, 1956; MCDONALD, 1942] both species, particularly the *P. aquatica*, showed to be associated, under certain environmental conditions and only in ruminants (sheep and cattle), with a typical complex of neurological disorders, commonly grouped under the term "phalaris staggers". The peracute syndrome or "sudden death", formerly included in the toxicosis complex, is now considered apart, owing to the etiology, almost certainly not tied to tryptamine alkaloids [BOURKE & CARRIGAN, 1992; BOURKE et al., 1988; BOURKE et al., 1992; GALLAGHER et al., 1964; 1966a; 1966b; KERR, 1972; MOORE et al., 1961; ORAM, 1970]. Nowadays most authors prefer to use the term "phalaris staggers" referring to the formerly separate acute and chronic syndromes, that seem to differ only for the duration of the exposure to the toxic agents [BOURKE et al., 1987; 1988; 1990; BRAUND, 1986; CULVENOR et al., 1964; CULVENOR, 1987; DE LAHUNTA, 1983; EAST & HIGGINS, 1988; GAGGINO et al., 1963a; 1963b; 1965; GALLAGHER et al., 1964; 1966a; 1966b; 1967a, 1967b; HARTLEY & KATER, 1965; HARTLEY, 1978; LEAN et al., 1989; LEE & KUCHEL, 1953a; 1953b; LEE et al., 1956; 1957a; 1957b; MCDONALD, 1942; MOORE et al., 1961; NICHOLSON, 1989; NICHOLSON et al., 1989; RENDIG et al., 1976; SIMPSON et al., 1969; ULVUND, 1985; WRIGHT et al., 1981]. The prodroms emphasize the neurological character of the disease: gait abnormalities, rigidity of the legs and then ataxia or weakness of the fore-limbs, muscular spasms, head nodding, depressed placing reflexes, convulsions, nystagmus, hyper-excitability, mydriasis, tachypnea, arrhythmic tachycardia. Death may occur by heart failure, few hours after the intake of toxic forage in the acute syndrome, until 5 months later in the chronic one [*ibid.*]. In the latter case, post-mortem examination gives evidence of irreversible degenerative lesion in the central nervous system. Macroscopically there are characteristic greyish-green deposits of pigments, particularly evident in the region of the geniculate bodies of the thalamus, in the ventral portion of the medulla oblongata at the level of the cerebellar peduncle and in the dorsal root ganglia.The same deposits are also found in the renal medulla and sometimes in the liver. The granular brown intracytoplasmatic pigments observed in the central nervous system and mainly accumulated in the lysosomes, are believed to be derived from the tryptamine alkaloids by oxidative deamination to aldehydes and self-condensation to melanin polymers. Microscopic degenerations, such as astrocytosis and secondary demyelination, followed the accumulation of the pigments in the cytoplasm, with a final

apparent death and lysis of the nerve cell body [BOURKE et al., 1990; EAST & HIGGINS, 1988; FERNANDEZ DE LUCO et al, 1990; GALLAGHER et al., 1964; 1966a; 1966b; HARTLEY & KATER, 1965; JOLLY & HARTLEY, 1977; LEAN et al., 1989; NICHOLSON, 1989; ULVUND, 1985; VAN HALDEREN et al., 1990].

The symptomatologic complex and the experimental administration of indole alkaloids to ruminants seem to support a direct action on the serotoninergic system by the *Phalaris* compounds (mainly indolalkylamines, even though it is not possible to exclude a synergic action by the ß-carbolines), [BOURKE et al., 1988; BOURKE et al., 1990] rather than a monoamine oxidase inhibition with consequent increase of the endogenous cathecolamines [GALLAGHER et al., 1966a; 1966b]. In this context, it is worth remembering that DMT and 5-MeO-DMT are not orally active in human beings and in general in non-ruminant animals, because of their inactivation in the digestive tract by the monoamine oxidase. The absorbtion of physiologically active amount of indole alkaloids in sheep and cattle would be therefore possible only in the rumen where evidently the inactivating process does not occur.

The economical importance of "phalaris staggers" and the more general negative influence of the indole alkaloids on the forage quality [ARNOLD & HILL, 1972; AUDETTE et al., 1970; BERRY & HOVELAND, 1956; BLOOD et al., 1983; BRINK, 1964; CARLSON et al., 1968; 1972; GALLAGHER et al., 1966a; 1966b; 1967; JORDAN & MARTEN, 1975; KENNEDY et al., 1986; KERR, 1972; MARTEN, 1973; 1981; MARTEN & JORDAN, 1974; MARTEN et al., 1976; 1981; NICHOLSON, 1989; NICHOLSON et al., 1989; O'DONOVAN et al., 1967; ODRIOZOLA et al., 1991; PARMAR, 1975; PARMAR & BRINK, 1976; ROE & MOTTERSHEAD, 1962; ROGLER, 1944; SIMONS, 1970; SIMONS & MARTEN, 1971; VAN ARSDELL et al., 1954; WILLIAMS et al., 1970; WITENBERG et al., 1992; WOODS, 1973; WOODS & CLARK, 1974] have been led up to a large number of chemical studies about the two main forage species in the genus *Phalaris*. From the work of WILKINSON [1958], who first reported in 1958 the presence of hordenine and 5-methoxy-N,N-dimethyltriptamine (5-MeO-DMT) in *P. arundinacea*, many other researches have been done [APPLESEED, 1993b; AUDETTE *et al.*, 1969; 1970; BALL & HOVELAND, 1978; BARNES *et al.*, 1971; BERG, 1978; JOHNSEN, 1978; COULMAN *et al.*, 1976; COULMAN *et al.*, 1977; CULVENOR *et al.*, 1964; DONKER *et al.*, 1976; DUYNISVELD *et al.*, 1990; FRAHN & O'KEEFE, 1971; FRAHN in KENNEDY *et al.*, 1986; FRELICH & MARTEN, 1972; FRELICH, 1973; FRELICH, 1972; GANDER *et al.*, 1975; HAGMAN *et al.*, 1975; HOVIN & MARTEN, 1975; JORDAN & MARTEN, 1976; KENDALL & SHERWOOD, 1975; MAJAK & BOSE, 1977; MAJAK *et al.*, 1978; 1979; MARTEN, 1981; MARTEN *et al.*, 1973; 1974; 1976; 1981; MCCOMB *et al.*, 1969; MOORE *et al.*, 1966; 1967; MULVENA & SLAYTOR, 1982; 1983; MULVENA *et al.*, 1983; ORAM & WILLIAMS, 1967; ORAM in KENNEDY *et al.*, 1986; ORAM, 1970; ISTREM & MARUM, 1989; ISTREM, 1987; PARMAR, 1975; PARMAR & BRINK, 1976; RENDIG *et al.*, 1970; 1976; SIMONS & MARTEN, 1971; SIMONS in BARKER & HOVIN, 1974; SIMONS, 1970; ULVUND, 1985; VIJAYANAGAR *et al.* 1975 (cf. also ; SHANNON & LEYSHON, 1971); WELCH, 1971; WILLIAMS *et al.*, 1971; WILLIAMS, 1972; WOODS & CLARK, 1971a; 1971b; WOODS *et al.*, 1979]. The alkaloids until now found in *P. arundinacea* and *P. aquatica* are:

- N-methyltryptamine (MMT)
- 5-methoxy-N-methyltryptamine (5-MeO-MMT)
- N,N-dimethyltryptamine (DMT)
- 5-methoxy-N,N-dimethyltryptamine (5-MeO-DMT)
- 5-hydroxy-N,N-dimethyltryptamine (Bufotenine, 5-OH-DMT)
- 5-methyl-tryptamine
- 5-methoxy-tryptamine
- 2-methyl-1,2,3,4-tetrahydro-ß-carboline (MTHC), not found in *P. aquatica*
- 2-methyl-6-methoxy-1,2,3,4-tetrahydro-ß-carboline (MMTHC)
- 2,9-dimethyl-6-methoxy-1,2,3,4-tetrahydro-ß-carboline (DMTHC)
- Gramine
- 7-methoxy-gramine
- 5,7-dimethoxy-gramine
- Hordenine

Some of the above-mentioned compounds, such as N-methyl-tryptamine, 5-methyltryptamine, 7-methoxy-gramine etc. are contained in the two species only in trace amount and they seem to be present exclusively in particular growing stages, probably as a part of the biosynthetical pathways of other indole alkaloids [MULVENA et al., 1983]. The ß-carbolines are also found in the two *Phalaris* in very low concentration, at most 5% of the indole alkaloids total amount, that is 0.0003% on the dry weight [AUDETTE *et al.*, 1969; 1970; FRAHN & O'KEEFE, 1971; GANDER et al., 1976; VIJAYANAGAR et al., 1975]. Such an unfavorable ratio of ß-carbolines/indolalkylamines makes

improbable (but maybe not impossible, particularly for some strains) the occurrence of the pharmacological conditions for carrying out an "*ayahuasca*-like effect" with only the *Phalaris* plants.

On the other hand the concentration of the other indole alkaloids, among which the psychoactive DMT and 5-MeO-DMT, is very variable. This variability, referred to both the absolute amount and the mutual relationship between the alkaloids, is influenced by many and often interacting factors.

In the first place, the capacity of producing indolalkylamines is genetically fixed. Many *P. aquatica* and *P. arundinacea* cultivars, under the same environmental conditions, differ considerably for quantity and type of alkaloids produced [BARKER & HOVIN, 1974; BROWN, 1961; COULMAN, 1977; COULMAN et al., 1976; DUYNISVELD et al., 1990; GANDER et al., 1975; HOVIN & MARTEN, 1975; MARTEN et al., 1976; MARUM et al., 1979; ORAM, 1970; ORAM & WILLIAMS, 1967; ØSTREM, 1987; SACHS & COULMAN, 1983; SIMONS, 1970; WOODS & CLARK, 1971a; 1971b]. This means that it is possible, as has been widely verified in the crop science, to select strains with low (and, obviously, high) alkaloids content. A genetical model has also been proposed [MARUM et al., 1979] which, even though it does not completely explain the relationships between the different classes of chemical compounds (probably affected by other factors), is valid according to the researches carried out in this field. The model proposes two dominant alleles controlling the phenotype T (synthesizing mainly DMT, MMT and MTHC) and M (containing 5-MeO-DMT, 5-MeO-MMT and MMTHC). The phenotype G, containing almost only gramine, would be produced when both the alleles are homozygous recessive. With regard to the biosynthesis, the double recessive *mmtt* would synthesize gramine from tryptophan through 3-aminomethylindole and 3-methyl-aminomethylindole; the genotypes *m* recessive/*T* dominant (*mmT*) would use the pathway tryptophan à tryptamine à MMT à DMT and MTHC (with a possible secondary pathway from DMT to MTHC); the genotypes *t* recessive/*M* dominant (*Mtt*) and *M* dominant/*t* dominant could use the pathway tryptophan à 5-methoxy-tryptophan à 5-methoxy-tryptamine à triptamine à 5-MeO-MMT (à derivation to MMTHC) à 5-MeO-DMT (à derivation to DMTHC) [*ibid.*; cf. also BAXTER & SLAYTOR, 1972a; 1972b; LEETE, 1967; MACK, 1974; MACK & SLAYTOR, 1974; 1976; 1978; 1979; 1988; SPENSER, 1970]

The greatest amount of indole alkaloids is found in the plant parts where the chlorophyllous activity is considerable [BALL & HOVELAND, 1978; FRELICH, 1973; HAGMAN et al., 1975; MARTEN, 1981; SIMONS & MARTEN, 1973; WELCH, 1971; WOODS et al., 1979]. The highest concentration is therefore contained in the leaf blades, particularly in the upper third of the seedling; on the contrary culm, panicle, quiescent leaves, leaf sheaths and hypogean parts show a low to very low content of indolalkylamines [*ibid.*; PARMAR, 1975; PARMAR & BRINK, 1976]. The total alkaloids concentration decreases with plant maturity [SIMONS & MARTEN, 1973; MARTEN et al., 1976; PARMAR & BRINK, 1976]; in some cases the decrease can be more than 50% during the progress from a vegetative stage to anthesis [FRELICH, 1973; FRELICH & MARTEN, 1972; SIMONS, 1970], even though for the latter maturity degree it is worth taking into account the larger weight of culms and panicles on the total biomass. In general, the total alkaloids and particularly the substituted tryptamines, are more concentrated in the first regrowth, after the cutting or grazing, than in the first growth just after the sowing, decreasing then in the following regrowths [BALL & HOVELAND., 1978; BARNES et al., 1969; 1971; COULMAN et al., 1977; DUYNISVELD et al., 1990; HAGMAN et al., 1975; MCCOMB et al., 1969; PARMAR & BRINK, 1976; WILLIAMS, 1972; WOODS et al., 1979]. It is worth noting that, whereas the above-mentioned trend and distribution in plant parts is generally valid for indole alkaloids (although with characteristic behaviours of the separate compounds), the non-indole alkaloid hordenine is normally more concentrated in the leaf sheath than in the blade and it follows a different trend during the maturity stages and the regrowths [COULMAN et al., 1977; DUYNISVELD et al., 1990; WOODS et al., 1979].

The availability of soil nitrogen increases the alkaloids concentration, particularly in cultivars with high alkaloids content, during the first growing stages and in plants growing in full sunlight [FRELICH, 1973; FRELICH & MARTEN, 1972; MARTEN, 1981; MARTEN et al., 1974; MOORE et al., 1966; 1967; PARMAR, 1975; PARMAR & BRINK, 1976; SIMONS, 1970; WELCH, 1971]. In these conditions, the addition of 120 kg/ha of nitrogen to a mixture of nitrogen-deficient peat and mineral soil produces an average total alkaloids increase of 50 % [MARTEN et al., 1974; MARTEN, 1984; SIMONS, 1970]. In soil, but not in nutrient solution cultivations, the concentration of indole alkaloids depends also from the source of nitrogen; in fact, the increase is greater in plants supplied with ammonium nitrogen compared to the nitric source [FRELICH, 1973; FRELICH & MARTEN, 1972; MARTEN, 1981; MARTEN et al., 1974; PARMAR, 1975; PARMAR & BRINK, 1976; WELCH, 1971].

The photoperiod has little influence on the production of alkaloids [FRELICH, 1973; FRELICH & MARTEN, 1972; MARTEN & FRELICH, 1977; MOORE et al., 1966; 1967; WILLIAMS, 1972] that is instead sensible to the shading. Samples of *P. arundinacea* growing with 20 % of the full sunlight can contain an amount of DMT about twice compared to the control; 5-MeO-DMT may increase up to a factor 25 [*ibid.*]. Regarding to the circadian oscillations, the DMT seems to show a maximum in the first hours of the morning, at least in the shaded plants, whereas the 5-MeO-DMT reaches a concentration peak in the late morning [WILLIAMS, 1972].

Plants growing after a moisture stress may contain up to three times the concentration of alkaloids found in regularly watered samples. The highest increase of the tryptamine alkaloids is shown at the first reduction of the leaves turgor: the most affected alkaloid seems to be the 5-MeO-DMT. Moreover, the first regrowth of the stressed plants contains more DMT and less 5-MeO-DMT than the regrowth of the non-stressed ones [MARTEN, 1981; WILLIAMS, 1972; cf. BALL & HOVELAND, 1978]. The influence of frost is very similar, even though in this case the DMT appears to be the most affected indole alkaloid. The highest increase for an exposure to -2°C during the night, is found in seedling of *P. aquatica* growing at high nitrogen level in the soil and with day/night temperature of respectively 21 and 16 °C [WILLIAMS, 1972]. There is, in conclusion, a little increase of the alkaloids in plants growing at high compared to low temperature but in general the effects of this factor are weak [FRELICH, 1973; FRELICH & MARTEN, 1972; MARTEN, 1981; MARTEN & FRELICH, 1977; MOORE et al., 1966; 1967; ORAM, 1970].

The almost satisfactory knowledge about the chemistry of *P. aquatica* and *P. arundinacea* demonstrates the wide interest to these species and the large number of researches dedicated to them. The situation is quite different, however, for the rest of the genus *Phalaris*. The only chemical study which analyzed the indole alkaloids in some species other than *P. aquatica* and *P. arundinacea* was, as far as we know, a research conducted by ORAM in 1970. The author studied 33 strains of 14 different entities but without specifying their identity. On this topic, the only results reported by Oram are the following:

- no species was entirely free of tryptamine alkaloids;
- the three species with chromosome number 2n=12 (probably *P. brachystachys, P. canariensis* and *P. truncata*) had low alkaloids level;
- *P. canariensis* always showed lower levels than any *P. aquatica* ecotype;
- variation in the alkaloid content was found between strains within *P. minor* and *P. arundinacea*.

Recentely, ODRIOZOLA and others (1991) did not find by thin layer chromatography any 5-MeO-DMT in toxic samples of *P. angusta* NEES ex TRIN., an American species. However, the authors reported an unidentified chromatographic spot producing the same color reaction as 5-MeO-DMT to Erlich's reagent, but having a different $R_f$ value; this compound could be DMT. As a confirmation that all or the most species within the genus *Phalaris* contain indolalkylamines, it has been reported that it is possible to produce livestock intoxications also for *P. angusta* NEES ex TRIN.*angusta* [ODRIOZOLA et al., 1991], *P. brachystachys* LINK in SCHRADER [FERNANDEX DE LUCO et al., 1990a; 1990b], *P. caroliniana* WALT. [NICHOLSON, 1989; NICHOLSON et al., 1989], *P. minor* L. [KELLERMAN et al., 1988; NICHOLSON, 1989; SCHNEIDER, 1978 (unpub. data) in VAN HALDEREN et al., 1990; VAN HALDEREN et al., 1990], and for the hybrid *P. aquatica X arundinacea* (also known as *Ronphagrass*) [VAN DER MERWE, 1959; RUELKE & MCCALL, 1961].

According to such information, in the summer 1993 we made some paper chromatographies regarding 10 samples from 5 species of cultivated *Phalaris*: *P.aquatica* L., *P.canariensis* L., *P.coerulescens* DESF., *P.paradoxa* L. and *P.truncata* L. The seeds of *P.aquatica, paradoxa* and *coerulescens* came from wild or naturalized places respectively in the province of Bologna, Livorno and Pisa (Central Italy). Other seeds of *P. coerulescens* and *P. truncata* came from the Botanical Garden of Bordeaux (France), whereas the ones of *P.canariensis* came from a commercial strain (Benary, Ziergröser, Germany). The seedlings were collected about 20-30 days after their germination. All the samples were found to contain indolalkylamines even though, lacking the chemical standards, the separate compounds were not identified [FESTI & SAMORINI, 1994]. During these preliminary researches we also undertook a semi-quantitative analysis on the total alkaloids extract of the wild *P. aquatica* strain, we will refer to as **AQ1**. The seeds, collected near Bologna, were cultivated in Rovereto (North Italy, latitude 46° north ca.). The total alkaloids fraction from the distal two thirds of the first regrow after the cutting, previously fertilized with ammonium sulfate, was extracted in accordance with the simple method described by "John Appleseed" in *Entheogen Review* [APPLESEED, 1992]. The weighing of the oily residue led us to estimate the alkaloids content to be greater than 1 % on dry weight.

These preliminary data has urged us to undertake, in 1994, a more specific research which aims at a chemical characterization of the European *Phalaris* and which is still going on. Seeds of *P.aquatica* L., *P. arundinacea* L., *P. brachystachys* LINK in SCHRADER, *P.canariensis* L., *P.coerulescens* DESF., *P. minor* RETZ., *P.paradoxa* L., *P. stenoptera* HACK. and *P.truncata* L., from different European botanical gardens or from authors' collections, were grown on commercial standard soil in Rovereto. One or two samples (first growth and regrowth after cutting) for each species were collected and sent to the chemist Fabio Calligaris, working at the University Institute of Chemistry in Turin, to whom we are grateful, for his precious collaboration. Some qualitative results of this analysis, mainly carried out by means of high pressure liquid chromatography (HPLC), will be presented here, while for the complete results and the experimental methods a specific publication will follow. Since the quantitative researches and the checks about the extraction method are still lacking, the following data must be considered absolutely preliminary, although they could give an idea on the species variability.

All the seven species analyzed so far contain DMT as the main alkaloid: however, *P. brachystachys* and *P. minor* seem to contain only this indolalkylamine, the former in high concentration, tha latter in trace amount. Bufotenine, or 5-OH-DMT, is found in very low quantity in all the other species. MMT is present in *P. paradoxa*, *P. truncata* and *P. aquatica* even though only in the last species it reaches significant concentrations. Also 5-MeO-DMT shows a scattered distribution among the analyzed samples, being present only in *P. truncata*, *P. canariensis* and *P. aquatica*. These data, in any case not definitive, seem to be only partially in accordance with the few above mentioned researches on the *Phalaris* other than *P. aquatica* and *P. arundinacea*. Therefore, we need the results of a wider spectrum of samples in order to go deeper into the topic. For the time being we can emphasize the importance of analyzing separately the presence of every single indolalkylamine in the plants. As a matter of fact, the total alkaloids content is not sufficient to understand the possible pharmacological activity as well as the variability and the chemiotaxonomic relationships among the *Phalaris* species.

## *Pharmahuasca* with *Phalaris aquatica* and *Peganum harmala*

Occasionally *P. aquatica* has been pointed out as a possible source of entheogenic indolalkylamines [DEKORNE, 1993b; 1994a; 1994c; FESTI & ALIOTTA, 1990; OTT, 1993; 1994a; SAMORINI, 1992] but until now and as far as we know, there are no published data about its use in *pharmahuasca* experiments.

On these grounds, we have paid particular attention to an Italian wild strain of *P. aquatica*, that we found interesting in the preliminary chemical analysis. This strain was first observed growing near Bologna and named **AQ1** by Giorgio Samorini. From a morphological point of view its characters are included in the variability limits of the species [cf. BALDINI, 1993], apart from the panicle tending to be a little longer at the plant maturity. However, its habitat is quite particular: AQ1 is in fact widespread on the *calanchi*, that is big furrows dug by the eroding water on clay hill soils, in general showing a very typical and interesting flora. As we have not pursued, until now, any systematic investigation about different Italian strains of *P. aquatica*, it is possible that the high alkaloids content of AQ1 is shared with other *P. aquatica* populations in Italy. On the other hand, the bibliographical data seem to show that there is not a correlation between alkaloids content of *Phalaris* wild strains and their geographical origin [ORAM & WILLIAMS, 1967; ORAM, 1970].

Seeds of AQ1 collected in its original habitat near Bologna, were sown in a field in Rovereto during the first spring months; the plants, regularly watered, were fertilized after the first cutting with ammonium sulfate in an amount equivalent to 200 kg/ha.

The first harvest, carried out 15 days after the sowing, could contain cyanogenetic compounds, even though in little concentration [GAGGINO et al., 1965], and so it was not used for the ingestion experiments. From a part of these young leaf blades the total alkaloids were extracted using the *Entheogen Review* method [APPLESEED, 1992]. About 100 mg of extract smoked with tobacco produced a clearly entheogenic experience. On the contrary, the effects of the smoke from dried young plants were scarcely perceptible and only perceived by one subject. However, it is worth remembering that the drying at room temperature or in a dryer at 40° C reduces the total alkaloids concentration by up to 50 % [CULVENOR et al., 1964; MARTEN, 1974 in DONKER et al., 1976; DONKER et al., 1976]. To this reduction we should add the partial destruction of the indole alkaloids owing to the direct burning. In this way, the amount of DMT or 5-MeO-DMT inhaled during the first mouthfuls is not enough to produce entheogenic effects but it succeeds in inducing tolerance, so blocking the possible action of the smoke subsequently inhaled. However, eliminating the causes

of the alkaloids loss, *P. aquatica* becomes completely active also by pulmonary way. In fact, some subjects reported a clearly entheogenic experience after inhalation of different amounts of the vapour emitted by heated (without combustion) fresh plant. It must be mentioned that the samples used in these experiments were cut from the second regrowth: this could be interpreted as further evidence for the AQ1 potency, since, in accordance with the bibliographical data, the alkaloids level decreases with the maturity [*vide supra*].

The upper part of the first regrowth (about 1.5 kg) was boiled in water acidified with citric acid to pH 4 for about half an hour; the water was enough to cover completely the vegetal material. After filtration, the residue was extracted once again with the same procedure. The resulting liquid was then reduced to a quarter by means of light heating. Seeds of *Peganum harmala* were separately extracted using the same method.

Lacking quantitative analysis about the strain AQ1 and even though we knew the wide variability of the *P. aquatica* alkaloids content, we had to refer only to the bibliographical data in estimating the approximate indolalkylamines amount to ingest during the experiments. This is the reason why the first experiment produced in one of us an effect that we could define as an alkaloids overdose. A *P. harmala* extract quantity corresponding to 4.5 g of seeds was first ingested on an empty stomach; the AQ1 extract supposed to correspond to 40 mg of indole alkaloids, but probably greater for at least a factor 5, and equivalent to about 400 g of fresh *Phalaris aquatica* was ingested 20 minutes later. A first peak, clearly entheogenic but fully controllable, became evident about 30 minutes later, followed by an apparent sensation of diminishing effects. In this first phase neither nausea nor any other physical symptoms or feeling to be intoxicated appeared. One hour and a half after the ingestion of *P. aquatica* the effects quickly became acute again leading, for one of us, to a complete loss of consciousness 40 minutes later. During this unconscious phase, that was resolved only 13 hours after the ingestion of *P. harmala*, we observed symptoms of adrenergic activation with strong mydriasis, muscular hypertonicity (particularly in the nape and the back), muscular clonus, tremors, exaggerated reflexes. These physical symptoms became less intense about 8 hours after the ingestion even though clonic movements and atavistic motor reflexes of clearly psychogenic origin still persisted. During the following days neither hangover nor other after-effects were observed, apart from the obvious tiredness the day after the experience. However, the oneiric activity was disturbed for the whole of the following week; this may be considered in accordance with the hypotheses proposed by CALLAWAY [1988] about the interaction between endogenous ß-carbolines and indolalkylamines as a possible base for the oneirogenic mechanism.

Starting from the results of this first attempt, in a second experiment a *Peganum harmala* extract amount corrisponding to about 2.5 g of seeds was ingested followed, after 20 minutes, by a quantity of AQ1 extract approximately corrisponding to 60 g of fresh *Phalaris* (that is less than 1/5 compared to the first experiment). After 5 minutes a frankly entheogenic experience began, with a peak after one hour and completely cleared up after 6 hours. The plateau was characterized by alternate phases of partial evanescence and rush of the effects.

In conclusion, verified the expected psychoactivity of *P. aquatica* either by pulmonar absorbtion or in the *pharmahuasca* combined with *Peganum harmala*, the results of these few, preliminar experiments need some considerations.

First of all, the oral psychoactivity of the *P. aquatica* integral aqueous extract is obviously different from those of the single compounds DMT or 5-MeO-DMT and maybe also from those of the total alkaloids extract from the plant. Moreover, in spite of the title of this communication where we use the word "*ayahuasca*-like effect", the *pharmahuasca P. aquatica/P. harmala* seems to be a lot different from the *Ayahuasca australis*: the sometimes aggressive and often up-down subjective effects of the former are in contrast with the meditative and often almost oneiric characteristic of the latter. The reasons for this difference are probably due to the distinct chemistry of the two preparations. It is possible that some pharmahuasca characters are linked to the interaction between DMT and 5-MeO-DMT considering that the latter substance is not contained in the classic additive *Psychotria viridis* RUIZ & PAVON [cf. OTT, 1993; 1994a]. We cannot exclude, however, that other compounds present in the *Phalaris*, little or not active themselves, could play an important role in the global pharmacology of these species.

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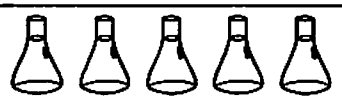
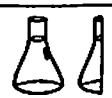
**Relative alkaloids content of some European *Phalaris*: preliminary data**

(HPLC analysis by Fabio Calligaris)

| | DMT | MMT | 5-Meo-DMT | 5-OH-DMT |
|---|---|---|---|---|
| P. aquatica (AQ1) |  |  |  |  |
| P. aquatica (Commercial) |  |  | |  |
| P. arundinacea (France) |  | | |  |
| P. brachystachys (Portugal) |  | | | |
| P. canariensis (Portugal) |  | |  |  |
| P. minor (Portugal) |  | | |  |
| P. paradoxa (Romania) |  |  | |  |
| P. truncata (France) |  |  |  |  |

 = Detectable amount

 = Trace amount