Pharmepéna-Psychonautics: Human Intranasal, Sublingual and Oral Pharmacology of 5-Methoxy-N,N-Dimethyl-Tryptamine†

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Abstract—Summarized are *psychonautic bioassays* (human self-experiments) of *pharmepéna*—crystalline 5-methoxy-N,N-dimethyltryptamine (5-MeO-DMT; O-Me-bufotenine), at times combined with crystalline β-carbolines (harmaline or harmine). These substances were administered via intranasal, sublingual and oral routes, by way of pharmacological modeling of diverse South American shamanic inebriants (principally the snuffs *epéna/nyakwana*, prepared from barks of diverse species of *Virola*.) Intranasal, sublingual and oral psychoactivity of 5-MeO-DMT, and the 1967 Holmstedt–Lindgren hypothesis of the *paricá-effect* —intranasal potentiation of tryptamines by concomitant administration of monoamine-oxidase-inhibiting (MAOI) β-carbolines from stems of *Banisteriopsis caapi* admixed with the snuffs—have been confirmed by some 17 psychonautic bioassays. Salient phytochemical and psychonautic literature is reviewed.

Keywords—harmaline, harmine, MAOI; 5-methoxy-DMT, shamanic snuffs, tryptamines

In previous articles modeling *ayahuasca* potions (Ott 1999; 1994), and *ñopo* (*Anadenanthera*) snuffs (Ott 2001), I confirmed the Holmstedt & Lindgren (1967) theory of synergetic interactions between tryptamines (DMT and bufotenine, respectively) and β-carbolines (harmine and harmaline) in these South American shamanic inebriants. In this third of four related articles, I report psychonautic bioassays of *pharmepéna*, modeling shamanic snuffs containing principally the obscure tryptamine O-methyl-bufotenine (5-MeO-DMT); a fourth article will model nicotine-containing tobacco-snuffs.

Epéna and *nyakwana* are generic terms most widely applicable *scientifically* to snuffs derived from barks, bark-exudates and bark-extracts of some seven species of *Virola* (Myristicaceae), which remain widely used in northwest Amazônia and the Orinoco region (Schultes 1984, 1979; Schultes & Holmstedt 1971, 1968). There is some evidence shamanic snuffs have been prepared from *Virola* leaves; this was reported once but not adequately documented (Ducke 1939), and *Virola* and related myristicaceous bark-extracts were formerly used orally or sublingually, now an obsolete practice (Boom & Moestl 1990; Schultes & Swain

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1976; Schultes et al. 1977; Schultes 1969). Also poorly documented is the ingestion of crude *Virola* saps (Schultes 1969), and smoking of *Virola* barks (McKenna, Towers & Abbott 1984; Schultes & Holmstedt 1971). *Virola* snuffs are also called *paricá*, a generic term for South American shamanic snuffs (as to a lesser extent is *epéna*) sometimes applied to those prepared from seeds of leguminous *Anadenanthera* (Ott 2001, 2000; Torres 1996; de Smet 1985a, b).

There are only four published reports of psychonautic bioassays of *Virola* inebriants. Schultes (1954) effectively discovered these shamanic snuffs with his detailed documentation of a Puinave *ya-keé* snuff on the Colombian Río Inirida, which included a bioassay—with but one-fourth the normal dose, which was nonetheless pharmacologically active, albeit not visionary. Schultes and Holmstedt (1971, 1968) later detailed the preparation and activity of a Waiká snuff (which was also used interchangeably as a dart poison) made from *Virola theiodora* (Spr. ex Benth.) Warb. Schultes noted the snuff scraped from dart points "has the same effect as the snuff that was made directly" (dramatically described by Davis 1996). Plotkin (1993a, b) recounted his highly visionary experience following insufflation of a Waiká *epéna* (*Virola*) snuff, which was combined also with a *hisiomi* (*Anadenanthera* seed) snuff; and McKenna documented oral (swallowed) bioassays of various *Virola* "pastes," none of which proved to be psychoptic. In this article I present my sublingual bioassays of a commercially-available *Virola* paste (see also Ott 2000).

Abundant chemical work on *Virola* consistently shows 5-MeO-DMT to be the most important tryptamine in barks of 12 species containing psychoptic tryptamines; DMT is found in the case of leaves (eight species); and there is an anomalous and poorly-documented report of bufotenine being found in seeds of *V. bicuhyba* (Schott) Warb., the resin of which is said to be psychoactive (Schultes & Holmstedt 1971; Teixeira da Fonseca 1922). In all, 15 tryptaminic species are known, of which seven contained merely traces, all of the remaining seven (setting aside *V. bicuhyba*, which is doubtless tryptaminic, despite lack of confirmation of bufotenine content) of known use in shamanic inebriants (McKenna, Towers & Abbott 1984; Holmstedt et al. 1980; Soares Maia & Rodrigues 1974; Lai et al. 1973; De Almeida Costa 1970; Agurell et al. 1969; Corothie & Nakano 1969; Holmstedt & Lindgren 1967). Eight studies of 11 samples of probable *Virola* snuffs showed 5-MeO-DMT to be the only tryptamine present in significant amounts. Quantitative data on seven *Virola* snuffs revealed 0.15% to 11.0% total tryptamines (average: 3.63%), with 5-MeO-DMT only in five samples, and two also having DMT (11:88 and 20:72, in relation to 5-MeO-DMT); the 11.0% sample contained 9.7% 5-MeO-DMT and 1.2% DMT (McKenna, Towers & Abbott 1984; Galeffi, Messana & Marini-Bettòlo 1983; Grossa et al. 1975; De Budowski et al. 1974; Chagnon, Le Quesne & Cook 1971; Agurell et al. 1969; Holmstedt & Lindgren 1967; Holmstedt 1965). There are a few phytochemical studies of eight "oral" pastes from three species of *Virola*. Again, all contained exclusively (in the case of *V. elongata* [Benth.] Warb. and *V. peruviana* [DC.] Warb.) or mainly 5-MeO-DMT (0.017% to 1.57%)—a sample of *V. sebifera* Aubl. paste contained 1.32%, along with 0.34% DMT (McKenna, Towers & Abbott 1984; MacRae & Towers 1984; Holmstedt et al. 1980). The psychoptic activity of 5-MeO-DMT taken as inhaled free-base vapor and via intravenous injection is well known (Shulgin & Shulgin 1997; de Smet 1983), but there is no published information on its activity as errhine or snuff, nor as taken sublingually; while it is orally active in *pharmahuasca* (viz., with concomitant ingestion of an adequate dose of MAOI; see Ott 1999 and 1994), it has been stated repeatedly (and erroneously) to lack oral activity when taken alone. Accordingly, I decided to investigate the intranasal, sublingual and oral pharmacology of this *epéna*-snuff tryptamine. All bioassays were conducted outside of the United States, by me alone. To my knowledge, 5-MeO-DMT is not a controlled substance in any country, although arguably in the U.S. it is a "controlled substance analogue."

MATERIALS AND METHODS

Harmine and harmaline hydrochloride dihydrate salts and 5-MeO-DMT free-base were purchased from Acros Organics (Geel, Belgium). A concentrated Peruvian *Virola* resin was supplied by Boris Crary of Tokyo, Japan. Intranasal, sublingual and oral bioassay methodologies have been detailed in a previous article in this series (Ott 2001).

5-MEO-DMT-INTRANASAL PSYCHONAUTICS (MN)

Six bioassays (MN-I—MN-VI) sufficed to model *Virola* shamanic snuffs. Insufflating 10 mg 5-MeO-DMT free-base (0.14 mg/kg) in MN-I established the intranasal visionary threshold, evoking a characteristic pharmacodynamic profile for this tryptamine taken as errhine: initial effects at three to four minutes, building to a peak between 35 and 40 minutes, clearly diminishing by 50 minutes, and effectively terminating by 60 to 70 minutes. Given the contrituration of *Banisteriopsis* liana with *Virola* snuffs, MN-II–MN-V involved combinations of *Banisteriopsis* β-carbolines with 5-MeO-DMT. The same 10 mg dose of 5-MeO-DMT was thus combined with 20, 10 and 5 mg (MN-II, MN-III, MN-IV) harmaline hydrochloride dihydrate (equal to 14.9, 7.5, 3.7 mg harmaline free-base; 0.21, 0.11, 0.05 mg/kg). In each case there was significant and dramatic potentiation of this threshold dose of 5-MeO-DMT, irrespective of the diminishing harmaline dose. MN-V was a control-experiment which consisted of insufflating simply 7.5 mg harmaline (as base-equivalent), which provoked no appreciable effects. In MN-VI, I

insufflated 5 mg 5-MeO-DMT (0.07 mg/kg) with 3.7 mg harmine (0.05 mg/kg base-equivalent), which provoked effects commensurate with MN-I (10 mg 5-MeO-DMT)—both β-carbolines roughly doubling the intranasal potency of 5-MeO-DMT.

5-MEO-DMT-SUBLINGUAL PSYCHONAUTICS (MS)

Like bufotenine (Ott 2001, 2000), sublingual 5-MeO-DMT proved to be equipotent with intranasal ingestion, having virtually the same pharmacodynamics, and being likewise susceptible to doubling of potency with similar doses of β-carbolines. In MS-I, 10 mg sublingual 5-MeO-DMT was virtually indistinguishable from that quantity intranasally (MN-I); likewise for MS-II and MS-III (10 mg 5-MeO-DMT taken with 7.5 and 3.7 mg harmaline base-equivalent, respectively). For MS-IV I halved the dose of 5-MeO-DMT to 5 mg, with 3.7 mg harmaline base-equivalent, which gave a threshold-level effect on a par with 10 mg 5-MeO-DMT neat, intranasally (MN-I) or sublingually (MS-I). A control-bioassay in MS-V involved taking 7.5 mg harmaline sublingually. Unlike the same quantity taken intranasally (MN-V), this elicited quite appreciable effects: a 12 to 15 minute incubation period, tinnitus at 18 minutes, peak at 35 to 40 minutes, and a feeling of "pharmacological possession" (neither stimulating nor sedating) diminishing by 45 minutes and fading away just after one hour. In MS-VI, I found that 3.7 mg of harmine base-equivalent was as effective as that quantity of harmaline (MS-III) at potentiating a 10 mg dose of 5-MeO-DMT; although unlike 7.5 mg harmaline sublingually (MS-V), 7.5 mg harmine sublingually in MS-VII was without effect. De Smet (1985a) reported no notable effects following insufflation of 0.5 mg/kg harmine free-base (some fivefold my own inactive intranasal dose of harmaline HCl in MN-V); nor could harmine be detected chemically in blood samples taken 15, 30, 60, 120 and 240 minutes post-ingestion.

VIROLA-PASTE-SUBLINGUAL PSYCHONAUTICS (VS)

McKenna (McKenna, Towers & Abbott 1984) had bioassayed (by swallowing) four *Virola* paste samples, only one of which (*V. elongata*, 1.57% 5-MeO-DMT) showed any activity at 1.5–2.0 g (equal to 23.6–31.4 mg 5-MeO-DMT; *ca.* 0.3–0.4 mg/kg), He noted: "considerable physiological distress rather than the perceptual and psychological [effects] typical of hallucinogens." Inasmuch as traditional use of such pastes has never been documented—Bora and Witoto informants being indeed "unclear and confused" as to which species of *Virola* had been employed as oral pastes by their "fathers and grandfathers" (Schultes 1979)—and insofar as similarly-confected Bora and Witoto tobacco pastes are *not* swallowed but rubbed onto buccal membranes, I conjectured (Ott 2000) that *Virola* pastes were designed for buccal absorption, *not* to be swallowed. The paste swallowed by McKenna contained two to three times the sublingual visionary threshold-level dose for 5-MeO-DMT.

Accordingly, I made three bioassays with a commercially-available *Virola* resin-concentrate, prepared according to Bora and Witoto methods, from Peruvian *cumala* bark (*V. calophylla* Warb., *V. callophylloidea* Markgr. or *V. peruviana*). In VS-I, I ingested sublingually a bolus of 1.0 g of this thick paste, coated in wood ashes. I began to feel a distinct tryptaminic activity at eight to 10 minutes, which failed to develop much (a subthreshold dose). For VS-II, I triturated 1.0 g of the paste with 7.5 mg harmaline base-equivalent and 0.25 g sodium bicarbonate, coating this bolus in cocoa-powder. This elicited a mild, threshold-level effect, much like MS-III (10 mg 5-MeO-DMT + 3.7 mg harmaline base-equivalent, sublingually). For VS-III, I doubled the dose to 2.0 g—two boli prepared as per VS-II. This gave a stronger tryptaminic effect, with additional pharmacological grace-notes.

5-MEO-DMT-ORAL PSYCHONAUTICS (MO)

It would be an exercise as tedious as invidious to enumerate the profusion of statements regarding the supposed lack of oral activity of 5-MeO-DMT. Only Shulgin & Shulgin (1997) have published results of an actual bioassay, of 35 mg, describing the experiment with only two words: "no activity," (having concluded the compound was "not orally active"). While their bioassay datum of course stands unchallenged, their conclusion was premature. In MO-I, I ingested 30 mg 5-MeO-DMT free-base (0.43 mg/kg) encapsulated, to preclude possible contact with my buccal mucosa. First activity, tinnitus, was evident at 12 minutes; euphoria and stimulation took place at 18 minutes; the peak occurred at around 40 minutes, clearly diminishing by 48 minutes; the "magical varnish" over the world all but evaporated at just past one hour. In intensity this was roughly commensurate with 10 mg 5-MeO-DMT (0.14 mg/kg) taken sublingually or intranasally (MS-I, MN-I), or 10 mg 5-MeO-DMT (by itself inactive) swallowed with 40 mg harmaline base-equivalent (0.57 mg/kg) in *pharmahuasca*. That is, 5-MeO-DMT is decidedly orally active, albeit at roughly one-third the potency as via intranasal, sublingual or *pharmahuasca* routes. In tests of a commercial *pharmahuasca* prototype, most subjects required 50% more harmaline—60 mg—to activate 10 mg 5-MeO-DMT in *pharmahuasca*, which indicates I tend toward the low gastric-MAO-phenotype. This might explain why 30 mg 5-MeO-DMT was orally active for me, whereas 35 mg was not for Shulgin & Shulgin; likewise as much as 31.4 mg for McKenna in a *Virola elongata* paste. In my case, some tenfold more harmaline (40 mg: 3.7 mg) had

been necessary to activate gastric 5-MeO-DMT via monoamine-oxidase inhibition, as had sufficed to potentiate this tryptamine bucally or intranasally; this suggests that dissolution in gastric juices, as opposed to nasal or buccal mucosa, is likely to expose 5-MeO-DMT to higher titers of MAO, or expose it for longer periods, or both.

DISCUSSION AND COMMENTARY

While referring the reader to my comprehensive book (Ott 2000) for background and fuller details on these bioassays, by way of summary I note that at least seven species of *Virola* are still used in northwest-Amazonian South America as snuffs, fumatories, masticatories and potions derived from the barks, and at least formerly were used as snuffs made from the leaves. Setting aside poorly-documented leafen snuffs (in which the important tryptamine is probably DMT), rather extensive phytochemical work points inexorably and consistently to 5-MeO-DMT as by far the major tryptamine in *Virola* barks and snuffs; these may contain substantial, albeit pharmacologically insignificant, amounts of DMT (which, by any route, is four to five times less active than 5-MeO-DMT). 5-MeO-DMT is of well-known psychoactivity, having been reported active by inhalation of free-base vapor in doses of six to 10 mg (Shulgin in de Smet 1983), and by intravenous injection in doses between two to three mg (Shulgin & Shulgin 1997). Despite its prominence as snuff-alkaloid, it appears nobody has experimented hitherto with its intranasal activity.

I think my evidence is conclusive and consistent—5-MeO-DMT, by far their major tryptamine, is the principal psychoptic agent of shamanic *Virola* preparations, whether snuffed, smoked, swallowed or sucked. Anyone with a modicum of tryptamine experience would have no difficulty distinguishing 5-MeO-DMT from bufotenine, although it has greater commonality with DMT. As inhaled free-base vapor it is roughly equipotent with bufotenine and some four- or five-fold more potent than DMT; taken as errhine or sublingually it is also some four- or five-fold more potent than DMT and also bufotenine. This generally holds for oral ingestion as well, with the proviso that orally, DMT requires activation by MAOI, whereas in sufficient dosage, both 5-MeO-DMT and bufotenine are impressively active orally by themselves. In Table 1 of my ***pharmahuasca*** article (Ott 1999), I summarized published human pharmacology of 5-MeO-DMT.

I have already described intranasal activity of bufotenine and other psychoptic tryptamines, and noted that these are generally active orally, the prominent exception being DMT (Ott 2001). While this article was under review, several colleagues reproduced my findings regarding intranasal and sublingual activity of 5-MeO-DMT, including their potentiation by β-carbolines, although its oral psychoactivity remains unreplicated. I have presented these results at conferences in Switzerland and México, leading to some informal and small-scale marketing of ***pharmepéna***, which has now been employed intranasally by some hundreds of individuals. By all accounts, this has taken the "entheogen scene" by storm, and appears to be wildly popular among tryptamine aficionados. Although many have also tried 5-MeO-DMT sublingually, and have confirmed its psychoactivity, this would seem to be less popular than intranasal ingestion.

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