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 (harmane 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 sniffs 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 paried-effect—intranasal potentiation of tryptamines by concomitant administration of monoamine-oxidase-inhibiting (MAOI) β-carbolines from stems of Banisteriopsis caapi admixed with the sniffs—have been confirmed by some 17 psychonautic bioassays. Salient phytochemical and psychonautic literature is reviewed.

Keywords—harmane, harmine, MAOI, 5-methoxy-DMT, shamanic sniffs, tryptamines

In previous articles modeling ayahuasca potions (Ott 1999; 1994), and ḃaño (Anadenanthera) sniffs (Ott 2001), I confirmed the Holmstedt & Lindgren (1967) theory of synergetic interactions between tryptamines (DMT and bufotenine, respectively) and β-carbolines (harmane and harmaline) in these South American shamanic inebriants.

In this third of four related articles, I report psychonautic bioassays of pharmepéna, modeling shamanic sniffs containing principally the obscure tryptamine O-methyl-bufotenine (5-MeO-DMT); a fourth article will model nicotine-containing tobacco-sniffs.

Epéna and nyakwana are generic terms most widely applicable scientifically to sniffs derived from barks, bark-exudates and bark-extracts of some seven species of Virola (Myristicaceae), which remain widely used in northwest Amazonia and the Orinoco region (Schultes 1984, 1979; Schultes & Holmstedt 1971, 1968). There is some evidence shamanic sniffs 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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There are only four published reports of psychonautic bioassays of Virola inebriants. Schultes (1954) effectively discovered these shamanic sniffs with his detailed documentation of a Puinave ya-keé sniff on the Colombian Rio Inirida, which included a bioassay—with but one-fourth the normal dose, which was nonetheless pharmacologically active, albeit not visionary. Schultes and Hofmestert (1971, 1968) later detailed the preparation and activity of a Waiká sniff (which was also used interchangeably as a dart poison) made from Virola theiodora (Spr. ex Benth.) Warb. Schultes noted the sniff scraped from dart points “has the same effect as the sniff that was made directly” (dramatically described by Davis 1996). Plotkin (1993a, b) recounted his highly visionary experience following insufflation of a Waiká epéna (Virola) sniff, which was combined also with a hisiomi (Anadenanthera seed) sniff; and McKenna documented oral (swallowed) bioassays of various Virola “pastes,” none of which proved to be psychotropic. 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 psychotropic tryptamines; DMT is found in the case of leaves (eight species); and there is an anomalously and poorly-documented report of bufotenine being found in seeds of V. biciuhya (Schott) Warb., the resin of which is said to be psychoactive (Schultes & Hofmestert 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. biciuhya, which is doubtless tryptaminic, despite lack of confirmation of bufotenine content) of known use in shamanic inebriants (McKenna, Towers & Abbott 1984; Hofmestert et al. 1980; Soares Maia & Rodrigues 1974; Lai et al. 1973; De Almeida Costa 1970; Agurell et al. 1969; Corothie & Nakano 1969; Hofmestert & Lindgren 1967). Eight studies of 11 samples of probable Virola sniffs showed 5-MeO-DMT to be the only tryptamine present in significant amounts. Quantitative data on seven Virola sniffs 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-Bettolo 1983; Grossa et al. 1975; De Budowski et al. 1974; Chagnon, Le Quesne & Cook 1971; Agurell et al. 1969; Hofmestert & Lindgren 1967; Hofmestert 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. peruviána [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; Hofmestert et al. 1980). The psychotrophic 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 sniff, nor as taken sublingually; while it is orally active in Pharmahausca (viz., with concomitant ingestion of an adequate dose of MAO; 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-sniff 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

Harline 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 sniffs. 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 sniffs, 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, 1
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 pair 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. calophylloides 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 pharmahusaca. That is, 5-MeO-DMT is decidedly orally active, albeit at roughly one-third the potency as via intranasal, sublingual or pharmahusaca routes. In tests of a commercial pharmahusaca prototype, most subjects required 50% more harmaline—60 mg—to activate 10 mg 5-MeO-DMT in pharmahusaca, 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 buccally 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 biosays, 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 banks, 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 banks 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 psychotropic 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 erthine 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 psychotopic 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.

REFERENCES


