the hoasca project update

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FROM JUNE 21 THROUGH JULY 6, 1993, an interdisciplinary medical research team from the United States, Finland, and Brasil converged on the city of Manaus, the capital of the state of Amazonia, Brasil. Their common objective was to conduct a biomedical investigation into the acute and chronic effects of the plant hallucinogen, hoasca, which is utilized in a ritual context by the União do Vegetal (UDV), a Brasilian syncretic religion. Members of the UDV engage in the ceremonial ingestion of this substance approximately three to four times per month.

a biomedical investigation into the acute and chronic effects of the plant hallucinogen, hoasca

As regular readers of the MAPS newsletter will already be aware, planning for this project was initiated in 1991, after one of the investigators (Dennis McKenna) attended a conference on hoasca hosted by the UDV. He encountered there an enthusiastic reception to his suggestion to conduct a biomedical investigation of the pharmacology of hoasca tea and the psychological dynamics of its users; this willingness to collaborate was accompanied by a pool of scientific and medical talent, as many members of the UDV were trained as physicians, psychiatrists, or health professionals. Following the 1991 conference, Dennis returned to the United States and began developing the proposal outlining the objectives of the study. Funding for the project was solicited through Botanical Dimensions, which acted as the sponsoring organization. Thanks to the generosity of both large and small donors, Botanical Dimensions managed to collect $75,000 to fund the costs of this initial, pilot study. The primary objectives of this study were as follows:

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- Qualitative and quantitative analyses of the composition of hoasca teas and their source plants.
- Assessment of the acute physiological and neuroendocrine effects of hoasca teas, and pharmacokinetic analysis of the metabolism of the major alkaloids in hoasca tea.
- Assessment of the long-term effects of hoasca teas on functions mediated by serotonin, the neurotransmitter system most directly effected by hallucinogens, including the hoasca alkaloids.
- Psychiatric assessment and psychological profiling of the long-term users of hoasca tea, and comparison with an age-matched control group of non-users.

In the early stages of planning this project, we decided to conduct the study at the Nucleo Caupari, the main UDV temple located in the Amazonian city of Manaus, Brasil. It was felt that the membership of the Nucleo Caupari reflected the appropriate demographics and provided an adequate sample pool of long-term users. Nucleo Caupari is one of the oldest Nucleos (parishes) in the UDV, and many of its members have been regular consumers of hoasca for years. Some of the members also had friends or siblings who were not participants in the UDV and did not use hoasca, so the difficult

challenge of finding the appropriate control subjects was greatly simplified by the decision to conduct the study in this Nucleo. The UDV provided us with 15 subjects with long-term use histories, as well as 15 matched controls who had never taken hoasca.

The final protocol utilized in the research study included investigations of multiple medical, biochemical, psychiatric, and neuropsychological parameters. These consisted of pre-investigation physical examinations and laboratory work-ups, structured psychiatric and diagnostic interviews (a psychological profiling instrument known as the CIDI was used for this purpose), neuropsychological testing (WHO-UCLA Auditory Verbal Learning Test), personality testing (Tridimensional Personality Questionnaire - TPQ), and platelet receptor binding profiles (5-HT2 and 5-HT uptake binding). All of the above assessments were carried out on UDV subjects and age-matched controls. In the UDV subjects (but not controls), we conducted semi-structured "life story" interviews, phenomenological assessment of the hoasca-induced state of consciousness (Hallucinogen Rating Scale - HRS), and measurement of acute medical parameters following hoasca ingestion (EKG, blood pressure, heart rate, respiratory rate, temperature, pupillary diameter). Plasma samples were collected at predetermined intervals from the subjects; these were frozen and returned to the United States for neuroendocrine measurements (assays of serial cortisol, prolactin, and growth hormone) and pharmacokinetic analyses (time course profile of plasma levels of DMT, harmine, and tetrahydroharmine, the major alkaloids of hoasca). In addition, samples of the hoasca tea used in the test procedures and the source plants used in its manufacture were collected for chemical analysis.

Preliminary data analyses of all testing has been completed except for the HRS, the phytochemical and pharmacokinetic measurements, and the platelet receptor binding assays. Dr. Rick Strassman of the University of New Mexico, who developed the Hallucinogen Rating Scale as a component of his work with DMT in human volunteers, will complete the analyses of the HRS data. The phytochemical and pharmacokinetic analyses will be conducted by Dr. Kym Faull of the UCLA Neuropsychiatric Institute, and platelet receptor profiles will be studied by Dr. J. C. Callaway of the University of Kuopio, Finland. Dr. Callaway also assisted with the field studies in Manaus. Phytochemical analyses of the hoasca teas and source plants will also be conducted by Dr. Jose Cabral, of the Department of Natural Products at INPA (Instituto Pesquisas do Amazonas) in Manaus.

The Brasilian research team included members from the Department of Psychiatry at the University of Rio de Janeiro, and scientists from the Department of Biology and Toxicology, University of Campinas, as well as physicians and nurses from the Hospital Amazonas in Manaus. The team leader, Dr. Glacus de Souza Brito, worked closely with the principle investigators from the U.S. in planning, coordinating, and carrying out the planned study. Largely as a result of Dr. de Souza's organizational efforts, we were able to exceed the original objectives outlined for the study by including measurements of several parameters which had been dropped from the original protocol due to a perception that the limited funds and time available would not accommodate their inclusion. Dr. de Souza was instrumental in arranging for much of this work to be done free of charge at University and hospital labs in Manaus and São Paulo. One of the principle investigators from the U.S. →

assessments were carried out on UDV subjects and age-matched controls

remarked that, "had this work been done in the States it would have taken two years and cost half a million dollars; as it was we managed to complete the field phase in under three weeks for around $40,000." Laboratory analyses for the pharmacokinetic study and the platelet receptor profiles are still pending, but the funds for the research have been allocated.

The results of the research will be formally reported in various peer-reviewed journals as they become available. Some highlights of the psychological assessments included the finding in the structured diagnostic interview (CIDI) that UDV subjects exhibited a greater degree of past (though not current) alcohol and substance abuse, affective disorders and phobias. Many of the subjects interviewed in the open-ended "life-story" format credited their joining the UDV and particularly their regular use of hoasca tea as the key factor enabling them to reform their previously dysfunctional lifestyle and to maintain a more stable lifestyle over many years. UDV subjects also displayed superior performance on the neuropsychological test (WHO-UCLA Auditory Verbal Learning Test) designed to assess memory, recall, attention, and verbal ability. Significant differences were also found between UDV subjects and controls in the personality profile. The Tridimensional Personality Questionnaire (TPQ) measures three dimensions of personality, Reward Dependence, Harm Avoidance, and Novelty Seeking. There were no differences between subjects and controls on the Reward Dependence dimension; however the Harm Avoidance category revealed the UDV subjects as having greater "confidence" as opposed to "fear of uncertainty," greater "gregariousness" as opposed to "shyness with strangers," greater "uninhibited optimism" as opposed to "anticipatory worry," and greater "vigor" as opposed to "fatigability and asthenia." On the Novelty Seeking scale, UDV subjects displayed greater "stoic rigidity," as opposed to "exploratory excitability," greater "regimentation" as opposed to "disorderliness," and greater "reflection" as opposed to "impulsiveness."

UDV subjects also displayed superior performance on the neuropsychological test

Plasma samples were collected and analyzed for cortisol and prolactin in the laboratory of Dr. Russell Poland in the Harbor-UCLA Medical Center. Both parameters showed a rapid augmentation of hormonal secretion following ingestion of hoasca tea, results consistent with what one would expect to find with a substance which potentiated the serotonergic neurotransmitter system. These results thus supported our hypothesis that hoasca acts primarily as a serotonergic agonist.

Preliminary investigations have been completed by Callaway on the platelet receptor binding profiles. Long-term changes in the density of the 5HT uptake carrier in platelets were assessed using ^{3}H-citalopram as a high-affinity ligand. The 5HT uptake carrier is a membrane-localized protein which functions in serotonin transport in the CNS. The ^{3}H-citalopram binding profiles in long-term drinkers of hoasca tea (greater than ten years) were compared against an equivalent number of age-matched control subjects who were not users of hoasca. The haosca-using group was found to have a significantly higher density of 5HT uptake binding sites (Bmax), with no apparent change in affinity (Kd). This finding was unexpected and its significance, if any, is presently a matter of speculation.

We owe a special debt of gratitude to Botanical Dimensions and its President, Kathleen Harrison, for consistent encouragement and support, and for providing the non-profit venue within which this project was funded and administered. The interdisciplinary investigation of important ethnomedical plants falls within the Botanical Dimension's mandate, and it is through research of this kind that it can begin to realize its objectives.

Future issues of the MAPS newsletter will report on the results of the clinical and biochemical investigations as they become available, and will also discuss plans, currently being developed, for future studies which will expand on the results of this initial, pilot study. •

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