Subject: FW: Noise from the North #3
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Conversation: Noise from the North #3

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Conversation: Noise from the North #3
Subject: Noise from the North #3

Dear Readers,

A few people confused ignorance with stupidity after reading News from the North #2, as if the meaning of these words were the same. This in itself is another good example of ignorance, and not necessarily stupidity. Ignorance is defined as a lack of knowledge, or the unawareness of something important. Stupidity is a lack of intelligence. The misapplication of EU hemp sampling regulations by officials in some Member States is a good example of ignorance, because these sampling regulations are complex and difficult to understand. I do not exclude the possibility of stupidity as a factor in this mess, but for now I would like to focus on the demonstrated ignorance that still exists. At least we can do something about that!

Our quote for this week comes from Marie Curie (1867-1934):

"Nothing in life is to be feared. It is only to be understood"

Last week, in Noise from the North #2, I sent you my article entitled "A More Reliable Evaluation of Hemp THC Levels is Necessary and Possible", which will be printed in the next issue of the Journal of Industrial

Hemp. This was to help in understanding EU Regulation No 796/2004, the inherent short comings in the methodologies and suggestions for improvement. If you are new to this listing, issues #1 and #2 are already posted and freely available at http://www.finola.com

Fear and ignorance are also responsible for facilitating the belief that a hemp variety can somehow spontaneously change into a drug-Cannabis variety, although there is no evidence to support this irrational opinion. Just as a person with blue eyes will not wake up one morning with brown eyes, hemp does not spontaneously change into drug-Cannabis. It just does not happen without cross-pollination, followed by selective breeding over several generations. To think that it does, or even to have a fear that this might be true, is a special kind of ignorance that may be compounded by stupidity. This is matter of scientific fact, not public policy, and must be understood from a rational point of view.

The production of THC and other cannabinoids is under genetic control, and may be influenced to only a small degree by the environment. This is why the EU crafted regulations that specify the sampling time of hemp according to flowering characteristics. A large number of plants are also taken to control for the natural heterogeneity in a variety. But it is not sufficient to simply gather the correct number of plants at an arbitrary time and run them though the analytical procedure to achieve a number. Somehow, the official sampler must also understand how to determine the correct time of sampling, which is practically impossible from the small bit of information that is provided in Section 2.1, Annex 1 of EU Regulation No 796/2004. There is no definition for the phrase “end of flowering”, which is certainly more difficult to determine that the onset of flowering, from a botanical point of view. In other words, it is very easy to see when a plant begins to flower, but much more complicated to determine some vague point that

could be universally described as the end of flowering. It is surprising that "end of flowering" is not at all defined in the regulation, and is basically left up to the person who goes out to collect the sample, who may or may not know anything about hemp, much less the botanical determination of its flowering characteristics.

This week, in Noise from the North #3, I continue to present information that will help in discussing the current politics of hemp in the EU, which are not simple or even logical at times. The special theme of this issue is CBD (cannabidiol), another major cannabinoid of interest. The two attached articles help us to understand why hemp cannot be effectively used for drug purposes. First, the levels of THC are simply too low in hemp, even in the most extreme examples. This point is clearly illustrated in the first article (Cannabis CBD/THC.pdf). Secondly, the higher levels of CBD in hemp will effectively attenuate the possibility of a psychoactive drug effect from the low levels of THC in hemp. In other words, nothing will happen even if someone were to try and use hemp for drug purposes. This point is clearly described in the second article (CBDreview.pdf).

The first attachment (Cannabis CBD/THC.pdf) is an excellent article by Dr. Karl Hillig and Professor Emeritus Paul Mahlberg, who show that the cannabinoid profiles of hemp varieties are significantly different from drug-Cannabis varieties. This is simply determined by the ratio of CBD to THC in these crops. The beauty of this analysis is three fold: 1) it can be made by the same analytical methodology described in Section 3.4 of Annex 1 of EU Regulation No 796/2004, 2) this analysis does not depend so heavily on a specified time of sampling and 3) there is not such a critical need to verify the concentration of the THC standard in the analytical procedure, which is a serious analytical pitfall that is not addressed by the current method.

One should ask, 'Why is this not already part of the

analytical procedure?' or even 'Why isn't this already part of a methodology to evaluate a crop for drug potential before it is even admitted to the EU list of subsidized hemp varieties?'. As far as laboratory work is concerned, it is even easier and more precise than the current methodology describe in Annex 1 of EU Regulation No 796/2004. Easier and more precise? Yes, it is, and because there is no need to worry so much about the time of sampling or verifying the THC standard, the officials who do this work would not actually have to try and learn how to do anything differently. This means that there would be no urgent need to develop an elaborate training system throughout the EU to try and teach people in 27 different Member States how to understand and apply the current list of complex methods in Annex 1 of EU Regulation No 796/2004. Unless, of course, the objective is to increase more jobs and confusion with the current regulation.

The second attachment (CBDreview.pdf) is a recent publication that reviews the pharmacology of CDB, which is the main cannabinoid in hemp. Aside from being a very effective anti-inflammatory agent, with absolutely no psychoactive potential, I was especially interested in the antipsychotic properties of CBD, which are also discussed in this article. Perhaps the CBD in hemp could even be used as a cure for cannabiphobia!

Currently, official sampling agents in at least some Member States have still not understood EU Regulation No 796/2004, and especially the methods described in Sections 2 and 3 in Annex 1 of EU Regulation No 796/2004. This has led to the misapplication of both sampling and analytical methodologies as an inevitable consequence of a legislation that is so complex and peculiar. There are even serious irregularities in the reporting of THC results from some Member States to the EU Commission. How has this regulation even evolve into this contorted mess of special interest methodologies?

These will be other topics of interest to explore in future issues of Noise from the North.

For now, the question still worth asking is this- ‘Who really benefits from these complex and peculiar regulations, which are apparently designed to provide low THC values for monoecious fiber hemp varieties from Central Europe?’.

Hmmmm, now who could that be?... Hmmmm... Let me think about it for a moment...

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A CHEMOTAXONOMIC ANALYSIS OF CANNABINOID VARIATION IN *CANNABIS* (CANNABACEAE)[1]

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Cannabinoids are important chemotaxonomic markers unique to *Cannabis*. Previous studies show that a plant's dry-weight ratio of Δ^9-tetrahydrocannabinol (THC) to cannabidiol (CBD) can be assigned to one of three chemotypes and that alleles B_D and B_T encode alloenzymes that catalyze the conversion of cannabigerol to CBD and THC, respectively. In the present study, the frequencies of B_D and B_T in sample populations of 157 *Cannabis* accessions were determined from CBD and THC banding patterns, visualized by starch gel electrophoresis. Gas chromatography was used to quantify cannabinoid levels in 96 of the same accessions. The data were interpreted with respect to previous analyses of genetic and morphological variation in the same germplasm collection. Two biotypes (infraspecific taxa of unassigned rank) of *C. sativa* and four biotypes of *C. indica* were recognized. Mean THC levels and the frequency of B_T were significantly higher in *C. indica* than *C. sativa*. The proportion of high THC/CBD chemotype plants in most accessions assigned to *C. sativa* was <25% and in most accessions assigned to *C. indica* was >25%. Plants with relatively high levels of tetrahydrocannabivarin (THCV) and/or cannabidivarin (CBDV) were common only in *C. indica*. This study supports a two-species concept of *Cannabis*.

Key words: cannabinoid; *Cannabis*; chemotaxonomy; evolution; genetics; taxonomy; tetrahydrocannabinol.

Cannabis (Cannabaceae) has been a source of fiber, food, oil, medicine, and inebriant since prehistoric times (Chopra, 1969; Schultes, 1973; Abel, 1980). Whether the genus consists of one or more species is a matter of divided opinion (Schultes et al., 1974; Small and Cronquist, 1976; Emboden, 1981). *Cannabis* strains cultivated for fiber and/or seed production (here referred to as hemp) are commonly differentiated from strains cultivated for medicinal or recreational use, but the evolutionary relationships between these two groups and between cultivated and wild or naturalized (feral) populations are not well understood. To further resolve these issues, a systematic investigation of genetic, morphological, and biochemical variation was conducted on a diverse collection of 157 *Cannabis* accessions grown in a common environment (Hillig, 2004, in press). Chemotaxonomic aspects of that investigation are reported herein. Qualitative and quantitative analyses of cannabinoid variation and a method of characterizing cannabinoid differences among populations based on a simple genetic model provide new evidence regarding the evolution and domestication of this socioeconomically important genus.

Cannabinoids are terpenophenolic compounds unique to *Cannabis*. They are produced by glandular trichomes that occur on most aerial surfaces of the plant (Dayanandan and Kaufman, 1976; Turner et al., 1978). Approximately 61 cannabinoids are known to exist, although some of these are breakdown products or artifacts (Schultes and Hofmann, 1980; Turner et al., 1980). The cannabinoids discussed in this paper are biosynthesized in an acidic (carboxylated) form and are decarboxylated upon heating and drying of harvested plant material (Doorenbos et al., 1971). They are here referred to in their decarboxylated form. Cannabigerol (CBG) is the direct precursor of cannabichromene (CBC), cannabidiol (CBD), and Δ^9-tetrahydrocannabinol (THC) (Taura et al., 19 Morimoto et al., 1997). A homologous series of c with propyl side-chains is biosynthesized from ca varin (CBGV), including cannabivarichromene (CB nabidivarin (CBDV), and Δ^9-tetrahydrocannabivari respectively (Fig. 1A–D) (Schultes and Hofmann, 1 and/or CBD are generally produced in greatest a However, THCV and less commonly CBDV may levels of THC and/or CBD in some plants (Baker et THC and THCV are primarily responsible for the effects of marijuana and hashish (McPartland a 2001).

Chemotaxonomy has a long history of use in the tion of *Cannabis* taxa. Lamarck (1785) emphasized inebriant potential of *C. indica* Lam. when he diffe from *C. sativa* L. Names and descriptions of othe species of *Cannabis* have been published (reviewed tes et al., 1974; Small and Cronquist, 1976). Of thes *ruderalis* Janisch. is commonly accepted. Small (1 sidered the amount of THC produced by *Cannabi* "extremely important" taxonomic character and chromatography (GC) to differentiate *indica* strain *tiva* strains on the basis of their THC content (Small stead, 1973a, b; Small et al., 1975; Small and 1976). Small and Cronquist (1976) favored a mo concept and assigned these two taxa to subspecies of

Numerous biochemical studies of *Cannabis* pla from achenes ("seeds") of known geographic origin reported (Fetterman et al., 1971; Fetterman and Tur Nordal and Braenden, 1973; Small and Beckstead, Turner et al., 1973; Turner and Hadley, 1973a, 1974 et al., 1974; Holley et al., 1975; Small et al., 197 and Fairbairn, 1977; Beutler and Der Marderosi Clark and Bohm, 1979; Turner et al., 1979; Fournier 1980; Hemphill et al., 1980; Veszki et al., 1980; de al., 1992). Forensic studies of *Cannabis* examined and hashish samples of known origin, grown in environments (Jenkins and Patterson, 1973; Pod

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1973; Baker et al., 1980, 1982; Barni-Comparini et

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SPECIAL A

Cannabidiol: from an inactive cannabinoid to a d with wide spectrum of action

Canabidiol: de um canabinóide inativo a uma dr com amplo espectro de ação

Antonio Waldo

Abstract

Objective: *The aim of this review is to describe the historical development of research on cannabidiol.* ***Method:*** *This review was on reports drawn from Medline, Web of Science and SciELO.* ***Discussion:*** *After the elucidation of the chemical structure of can 1963, the initial studies showed that cannabidiol was unable to mimic the effects of Cannabis. In the 1970's the number of p on cannabidiol reached a first peak, having the research focused mainly on the interaction with delta9-THC and its antiep sedative effects. The following two decades showed lower degree of interest, and the potential therapeutic properties of c investigated were mainly the anxiolytic, antipsychotic and on motor diseases effects. The last five years have shown a remarkab in publications on cannabidiol mainly stimulated by the discovery of its anti-inflammatory, anti-oxidative and neuroprotective eff studies have suggested a wide range of possible therapeutic effects of cannabidiol on several conditions, including Parkinso Alzheimer's disease, cerebral ischemia, diabetes, rheumatoid arthritis, other inflammatory diseases, nausea and cancer. C In the last 45 years it has been possible to demonstrate that CBD has a wide range of pharmacological effects, many of whi great therapeutic interest, but still waiting to be confirmed by clinical trials.*

Descriptors: *Cannabidiol; Cannabis; Cannabinoids; History; Therapeutic uses*

Resumo

Objetivo: *O objetivo desta revisão é descrever a evolução histórica das pesquisas sobre o canabidiol.* ***Método:*** *Esta revisão foi utilizando-se bases de dados eletrônicas (Medline, Web of Science e SciELO).* ***Discussão:*** *Após a elucidação de sua estrutur em 1963, os estudos iniciais do canabidiol demonstraram que ele não foi capaz de mimetizar os efeitos da maconha. Na 70, o número de publicações sobre o canabidiol atingiu um primeiro pico, com as investigações centrando-se principalme interação com o delta9-THC e nos seus efeitos antiepiléptico e sedativo. As duas décadas seguintes apresentaram um men interesse e as propriedades terapêuticas potenciais do canabidiol investigadas foram, principalmente, as ansiolíticas, antip seus efeitos sobre as doenças motoras. Os últimos cinco anos têm demonstrado um notável aumento de publicações sob bidiol, principalmente estimulado pela descoberta dos seus efeitos anti-inflamatório, anti-oxidativo e neuroprotetor. Estes e sugerido uma vasta gama de possíveis efeitos terapêuticos da canabidiol em várias condições, incluindo doença de Parkins de Alzheimer, isquemia cerebral, diabetes, náusea, câncer, artrite reumatóide e outras doenças inflamatórias.* ***Conclusão:*** *N 45 anos, foi possível demonstrar uma vasta gama de efeitos farmacológicos do canabidiol, muitos dos quais são de grand terapêutico, que ainda necessitam ser confirmados por estudos clínicos.*

Descritores: *Canabidiol; Cannabis; Canabinóides; História; Usos terapêuticos*

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