

Vecchie e nuove droghe



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(Verona, 1 giugno 2007)

Brief overview of drug abuse history

- ❑ 1964-8: probably starts the psychedelic era
- ❑ 1968: S Francisco Summer of Love (J Joplin; J Hendrix): MDA, THC, LSD
- ❑ 1971-2: heroin finally arrives to Europe
- ❑ 1970s: 'soft' and 'hard' drugs
- ❑ 1981, NEJM: 6 AIDS cases first reported
- ❑ 1985: HIV positivity is a reality in Europe
- ❑ 1987-8: Ibiza
- ❑ 1990's: recreational/polydrug scene
- ❑ 2000-....: stimulants; Internet and the 'novel' psychedelics

La storia di uno psiconauta

SUMMARY

Uppers: Cocaine; Amphetamines; Cathinones

Downers: Benzodiazepines✓; Opiates✓; Alcohol✓
Barbiturates; Kava-Kava

All Arounders: LSD; Mescaline; DMT; Yage; Ayahuasca
PCP; Ketamine; MDMA; MDA; THC✓;
Ibogaine.

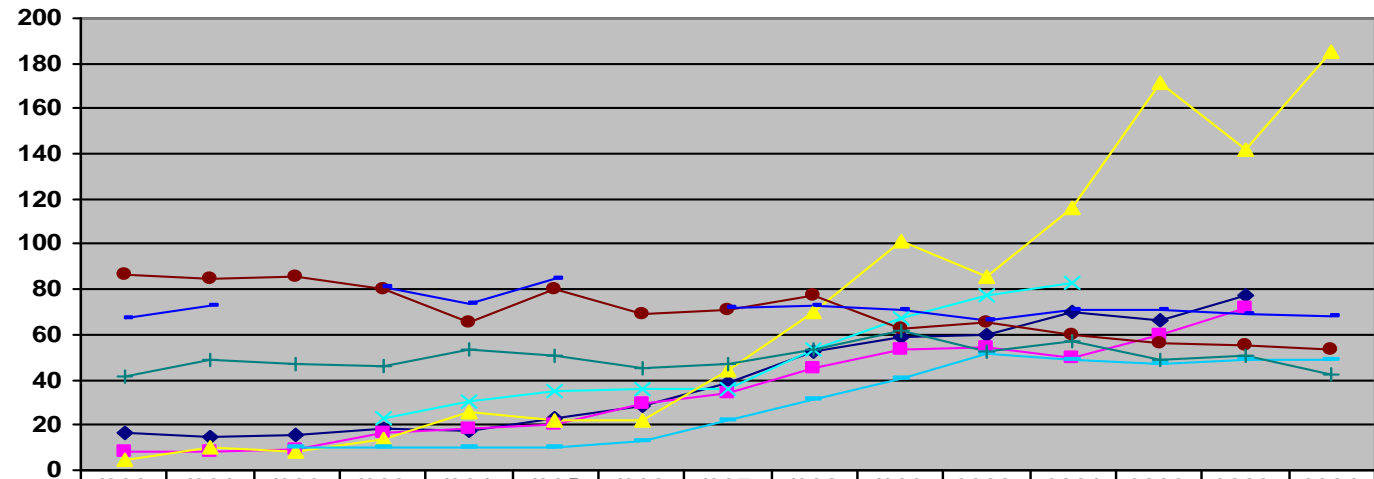
(✓ current use).

Cocaine: the available formulations

- ❑ The cocaine powder (hydrochloride) can be snorted; low bioavailability levels. It can be injected as well but.....
- ❑can't be smoked (because it decomposes at high temperatures). The alkaloid part is freed from the base through the use of ether. The result of this process is known as 'free-basing'.....
- ❑ ...and another form of 'free-basing' is called 'crack'. The HCl powder is heated with baking soda and water. Pure cocaine crystals are obtained. Both a quicker and a stronger 'high' and a shorter duration of action are reported.
- ❑ I.V. use of crack: use of citric acid

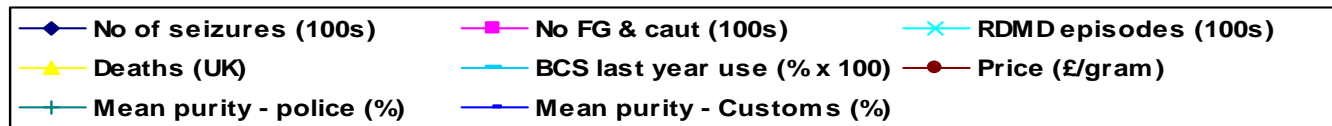
15 years of cocaine in the UK (Schifano and Corkery, 2006; Schifano and Corkery 2007)

Cocaine indicators, 1990-2004



| | 1990 | 1991 | 1992 | 1993 | 1994 | 1995 | 1996 | 1997 | 1998 | 1999 | 2000 | 2001 | 2002 | 2003 | 2004 |
|-------------------------------|-------|-------|------|-------|-------|-------|-------|-------|-------|-------|-------|-------|------|-------|-------|
| ◆ No of seizures (100s) | 16.36 | 14.46 | 15.5 | 18.26 | 17.28 | 22.7 | 28.21 | 38.37 | 52.09 | 58.58 | 60.05 | 70 | 66.4 | 77.44 | |
| ■ No FG & caut (100s) | 8.6 | 8.38 | 9.13 | 16.71 | 18.04 | 20.73 | 29.47 | 33.86 | 44.76 | 53.6 | 54.7 | 49.5 | 59.9 | 72.3 | |
| ✕ RDM D episodes (100s) | | | | 23.31 | 30.28 | 35.48 | 35.93 | 36.13 | 53.87 | 67.56 | 77.47 | 83.27 | | | |
| ▲ Deaths (UK) | 5 | 10 | 8 | 14 | 26 | 22 | 22 | 44 | 70 | 101 | 86 | 116 | 171 | 142 | 185 |
| — BCS last year use (% x 100) | | | 10 | 10 | 10 | 10 | 13 | 22 | 31 | 41 | 52 | 49 | 47 | 49 | 49 |
| ● Price (£/gram) | 87 | 84.6 | 86 | 80 | 65 | 80 | 69 | 71 | 77 | 63 | 65 | 60 | 56 | 55 | 53 |
| + Mean purity - police (%) | 41.25 | 49.25 | 47 | 46.5 | 53.25 | 50.5 | 45.5 | 47.4 | 53.75 | 62 | 52.2 | 57.5 | 48.5 | 50.97 | 42.63 |
| — Mean purity - Customs (%) | 67.5 | 72.5 | | 81 | 74 | 85 | | 71.57 | 72.8 | 71 | 66.6 | 70.9 | 70.9 | 69.16 | 68.19 |

Year



Ketamine, Special K

- ❑ Ketamine is a dissociative anaesthetic used primarily in veterinary practice. It may be injected, swallowed, snorted, or smoked
- ❑ Like phencyclidine, ketamine interacts with the N-methyl-D-aspartate channel. Analgesic effects occur at lower doses and amnestic effects at higher doses. Toxic effects include confusion and hostility

GHB; Liquid XTC

- GHB, a naturally occurring fatty acid derivative of gamma-aminobutyric acid, was introduced as a dietary supplement. Increasing doses progressively produce amnesia, drowsiness, dizziness, euphoria, seizures, coma, and death

Date rape drugs

- ❑ Dating violence is perpetrated by both males and females and occurs frequently within heterosexual dating relationships
- ❑ Alcohol, flunitrazepam, ketamine, and GHB have been used to facilitate sexual assault

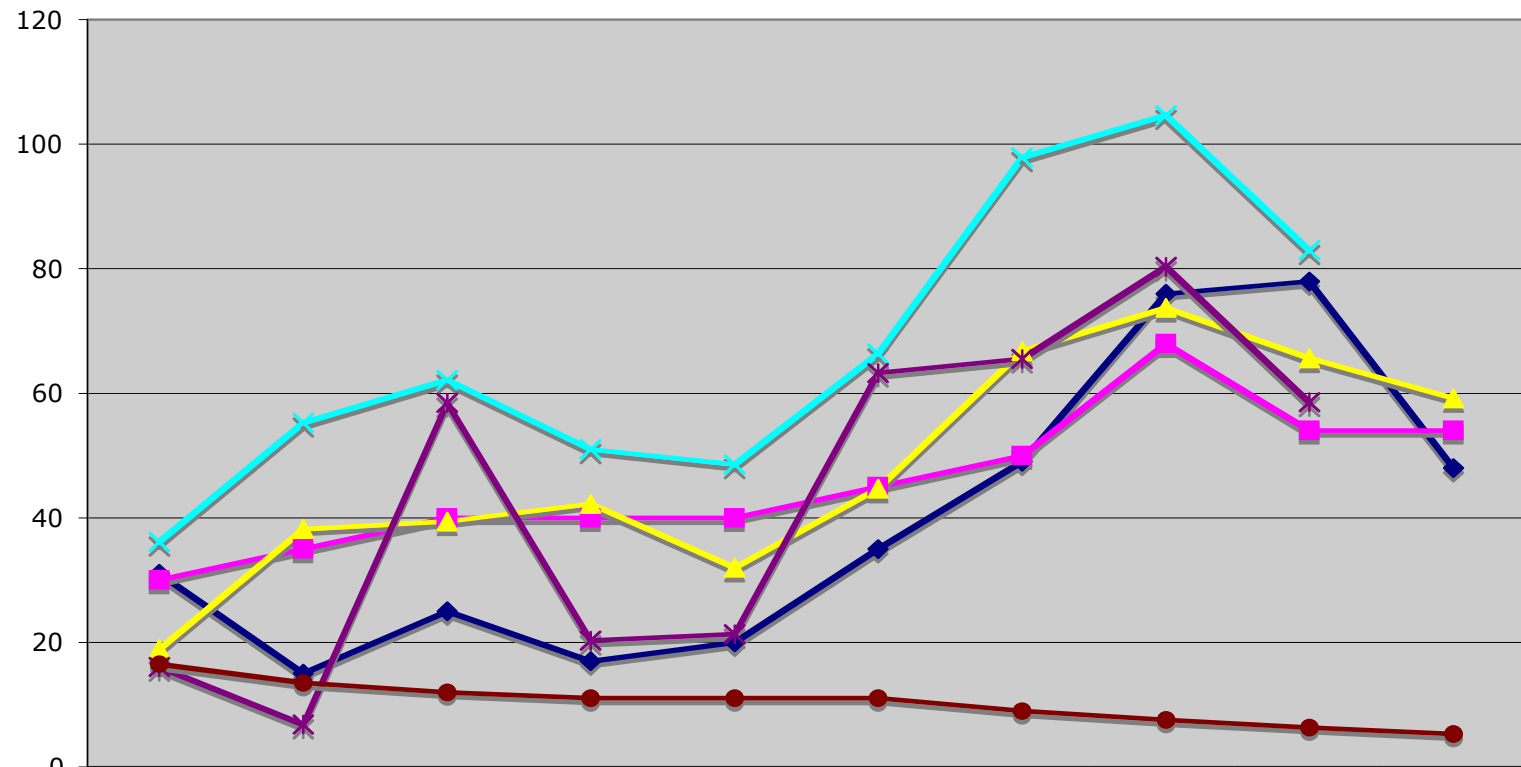
Smokable methamphetamines; “Crystal meth” (Schifano et al, in press)

- ❑ An extremely powerful stimulant.
- ❑ Causes an intense high that includes increased energy, talkativeness, and excitement
- ❑ Users are very unpredictable and can easily turn from euphoric to violent.
- ❑ Post-high low can lead to dependence

Crystal meth possible psychopathological consequences

- ❑ Anxiety, depression and insomnia
- ❑ Inability to function socially
- ❑ Paranoid thoughts; hallucinations; psychotic behaviour
- ❑ Homicidal and suicidal thoughts

Ecstasy in the UK, 1994-2003 (Schifano et al, J Psychopharmacol, 2005)



| | | | | | | | | | | |
|---------------------------|--------|--------|--------|--------|--------|--------|--------|---------|--------|--------|
| ◆ Death mentions | 31 | 15 | 25 | 17 | 20 | 35 | 49 | 76 | 78 | 48 |
| ■ BCS (%) x10 | 30 | 35 | 40 | 40 | 40 | 45 | 50 | 68 | 54 | 54 |
| ▲ Offenders (100s) | 18.810 | 38.210 | 39.370 | 42.210 | 31.960 | 44.700 | 66.700 | 73.700 | 65.600 | 59.200 |
| ✕ No. seizures (100s) | 36.140 | 55.210 | 62.160 | 50.980 | 48.500 | 66.370 | 97.840 | 104.600 | 83.000 | |
| * Doses seized (100,000s) | 15.982 | 6.775 | 58.480 | 20.290 | 21.273 | 63.296 | 65.500 | 80.300 | 58.520 | |
| ● Price (£) | 16.5 | 13.5 | 12 | 11 | 11 | 11 | 9 | 7.5 | 6.33 | 5.3 |



Searching the web for MDMA

(Deluca and Schifano; Am J Addictions, in press)



The Psychonaut 2002 EU project

Website: <http://www.psychonaut2002.org>

Searching the web for MDMA (1)

(Deluca and Schifano, Am J Addictions, in press)

- ❑ No studies have addressed the issue of what is available to the average web user in terms of information on MDMA.
- ❑ 280 web pages generated by two search engines in running queries for MDMA (ecstasy) were investigated.
- ❑ queries were carried out in English using a single generic keyword (MDMA) on the week starting on June 23rd, 2003
- ❑ The Google™ and AltaVista™ search for MDMA-(ecstasy) related websites respectively provided a list of 71,400 and 48,747 webpages. The first 100 websites identified by both search engines, together with a further random sample of 5% of the remaining sites (101 to 1,000) were fully assessed.
- ❑ Of the 280 webpages links, 23 were offline or with restricted access at the time of their assessment, thus reducing the sample to 257.
- ❑ Google™ showed a statistically significant difference between relevant and irrelevant websites' ranking ($p < .02$).

Searching the web for MDMA (2)

websites' position towards drug use:

- 50.4% anti drug
 - 16.2% harm reduction
 - 24.8% pro drug.
-
- MDMA pro drug websites showed a lower ranking (average value: 40.34 +/- 32.5), hence appearing significantly earlier in the results' list, than both the anti drug (55.0 +/-26.6) and the harm reduction (54.25 +/- 22.9) websites (p= .022).
 - Health professionals may need to be aware of the web being a new drug resource for at-risk information on MDMA.

PIHKAL (Shulgin and Shulgin), A chemical love story

Erowid Online Texts : PIHKAL #109 MDMA

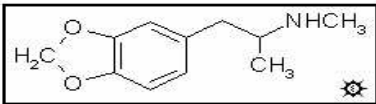
http://www.erowid.org/library/books_online/pihkal/pihkal109.shtml

PIHKAL A CHEMICAL LOVE STORY
ALEXANDER & ANN SHULGIN
hosted by erowid.org

← BACK MAIN INDEX TIHKAL FORWARD →

#109 MDMA

MDM; ADAM; ECSTASY; 3,4-METHYLENEDIOXY-N-METHYLAMPHETAMINE



[\[3D .jpg image\]](#)
[\[3D .mol structure\]](#)

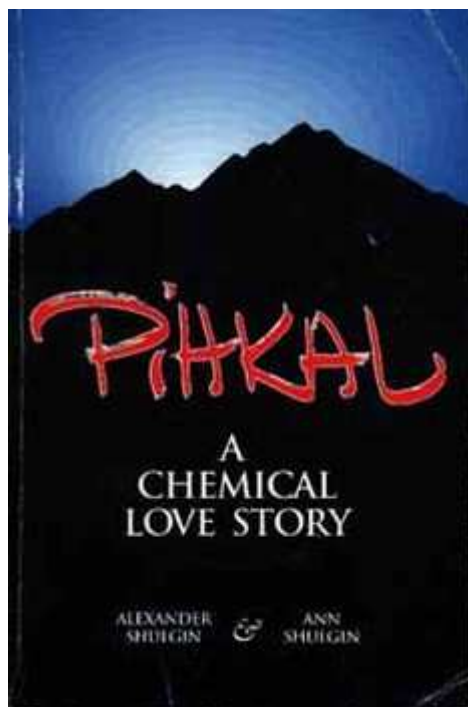
SYNTHESIS: (from MDA) A solution of 6.55 g of 3,4-methylenedioxyamphetamine (MDA) as the free base and 2.8 mL formic acid in 150 mL benzene was held at reflux under a Dean Stark trap until no further H₂O was generated (about 20 h was sufficient, and 1.4 mL H₂O was collected). Removal of the solvent gave an 8.8 g of an amber oil which was dissolved in 100 mL CH₂Cl₂, washed first with dilute HCl, then with dilute NaOH, and finally once again with dilute acid. The solvent was removed under vacuum giving 7.7 g of an amber oil that, on standing, formed crystals of N-formyl-3,4-methylenedioxyamphetamine. An alternate process for the synthesis of this amide involved holding at reflux for 16 h a solution of 10 g of MDA as the free base in 20 mL fresh ethyl formate. Removal of the volatiles yielded an oil that set up to white crystals, weighing 7.8 g.

A solution of 7.7 g N-formyl-3,4-methylenedioxyamphetamine in 25 mL anhydrous THF was added dropwise to a well stirred and refluxing solution of 7.4 g LAH in 600 mL anhydrous THF under an inert atmosphere. The reaction mixture was held at reflux for 4 days. After being brought to room temperature, the excess hydride was destroyed with 7.4 mL H₂O in an equal volume of THF, followed by 7.4 mL of 15% NaOH and then another 22 mL H₂O. The solids were removed by filtration, and the filter cake washed with additional THF. The combined filtrate and washes were stripped of solvent under vacuum, and the residue dissolved in 200 mL CH₂Cl₂. This solution was extracted with 3x100 mL dilute HCl, and these extracts pooled and made basic with 25% NaOH. Extraction with 3x75 mL CH₂Cl₂ removed the product, and the pooled extracts were stripped of solvent under vacuum. There was obtained 6.5 g of a nearly white residue which was distilled at 100-110 ° C at 0.4 mm/Hg to give 5.0 g of a colorless oil. This was dissolved in 25 mL IPA, neutralized with concentrated HCl, followed by the addition of sufficient anhydrous Et₂O to produce a lasting turbidity. On continued stirring, there was the deposition of fine white crystals of 3,4-methylenedioxy-N-methylamphetamine hydrochloride (MDMA) which were removed by filtration, washed with Et₂O, and air dried, giving a final weight of 4.8 g.

(from 3,4-methylenedioxyphenylacetone) This key intermediate to all of the MD-series can be made from either isosafrole, or from piperonal via 1-(3,4-methylenedioxyphenyl)-2-nitropropene. To a well stirred solution of 34 g of 30% hydrogen peroxide in 150 g 80% formic acid there was added, dropwise, a solution of 32.4 g isosafrole in 120 mL acetone at a rate that kept the reaction mixture from exceeding 40 ° C. This

PIHKAL Phenethylamines I Have Known And Loved

1991; 179 PEAs



'Entactogens/empathogens': the XTC-like drugs

- ❑ **MDA** ('love drug', the parental compound of MDMA)
- ❑ **MDEA** ('Eve', which has effects similar to those of MDMA)
- ❑ **MBDB** ('TNT')
- ❑ **2-CB** (*'nexus'*)
- ❑ **BOD** (allegedly providing yourself with '...16 hours of inner strength, good mood and contentedness')
- ❑ **DOB** (reported to be 33 times more powerful than MDMA itself; effects would last for up to 24 hours)
- ❑ **4-MTA** ('flatliners'; likely to be the result of the work of some researchers who were looking for new serotonergic agents)
- ❑ **2C-T-7** ('Blue Mystique'; created by A Shulgin and also one of his personal favourites). There is a complete series of 2C-T compounds (which includes **2Ci**, **2C-T-2** etc), either been synthesized already or just theorised



The Psychonaut 2002 EU project

(<http://www.psychonaut2002.org>)

...Let's buy some
'Blue Mystic'

The screenshot shows a web browser window displaying the JMAR CHEMICAL website. The browser's address bar shows the URL <https://www.jmarchemical.com/25dme.html>. The website header includes the company name "JMAR CHEMICAL" and contact information: "CONTACT 1.732.948.1906 / 9AM-5PM EST M-F". Below the header, there is a navigation menu with "HOME" and "ORDER" buttons. The main content area features a "PRODUCTS" section for "PD102", which is "2,5-DIMETHOXY-4-ETHYLPHENETHYLAMINE 4-ethyl-2,5-Dimethoxyphenethylamine hydrochloride". The product details include the CAS number (71539-34-9), formula (C12H19NO2), molecular weight (FW: 289.288), and purity (99.5+%). A chemical structure diagram of the compound is shown. The price list indicates: "C 500mg - \$148.00", "D 1g - \$264.00", and "F 5g - \$989.46". A "Related:" section lists several other products, including Phenethylamine, 2,5-Dimethoxyphenethylamine, 2,5-Dimethoxy-4-chlorophenethylamine, 2,5-Dimethoxy-4-(2-(4-ethoxythio)phenethyl)phenethylamine, 2,5-Dimethoxy-4-ethylthiophenethylamine, and 2,5-Dimethoxy-4-methylphenethylamine. At the bottom of the product page, there are buttons for "ORDER NOW", "PRODUCTS INDEX", "REQUEST A QUOTE", and "REGISTER". A "Login for full catalog" link is also present.

The 2C-T compounds

- ❑ 2C-T-7 is the most famous of a group of 24 compounds
- ❑ 2C-T compounds have structural and pharmacodynamic properties similar to other phenethylamine hallucinogens (mescaline, MDMA, PMA, 2C-B) and to indoleamine hallucinogens (LSD, psilocybin)

Nexus and Rachael

The latest generation of replicants (*Nexus-6*) are virtually indistinguishable from humans. While replicants can outperform humans physically and even mentally, they possess two **achilles heels**: a programmed four-year lifespan and ***the inability to show empathy***. This latter weakness forms the basis for discriminating them from humans via a Voight-Kampff (VK) *test of empathic responses* to carefully worded questions and statements

Rachael: Her primary natural attribution is the spider, Deckard's knowledge of which proves to Rachael that she is a replicant. The spider is the Great Mother in her aspects and the genetrix who spins the web of life from out of her own substance. Rachael can certainly be considered the weaver of Deckard's fate. As the Great Mother, Rachael is also ***Eve***.

2C-B



Synthesized by A Shulgin (California) in the early '70s

Distribution of the hallucinogen 2C-B has been sporadic since it became a Schedule I drug in 1995.

Since 1999, however, seizures of this drug have increased.

What are other names for 4-bromo-2,5-dimethoxyphenethylamine?

Nexus

Bromo
Performax
Spectrum

Venus

Erox
Cloud Nine
Cee-Beetje
BDMPEA

2C-B

Toonies
2's
Synergy

Eve

Zenith
Utopia
Afterburner Bromo
MTF

Practical info on 2C-B; Nexus

- can be ingested orally in its pill and capsule forms or "snorted" in its powder form. Users report that 2C-B's effects are more intense when it is snorted.
- Some users consume 2C-B in combination with other illicit drugs including MDMA (called a "party pack") and LSD (referred to as a "banana split").
- 2C-B produces euphoria and increased visual, auditory, olfactory, and tactile sensations.
- Doses of 20 to 30 milligrams result in very overt hallucinations. Even higher doses will produce extremely frightful, LSD-type hallucinations and morbid delusions.
- Proponents of its use consider the drug to be both a psychedelic and an "entactogen" ("touching within"). At low doses, users report feeling "in touch with themselves and their emotions" and often report erotic sensations

Effects of 2C-B



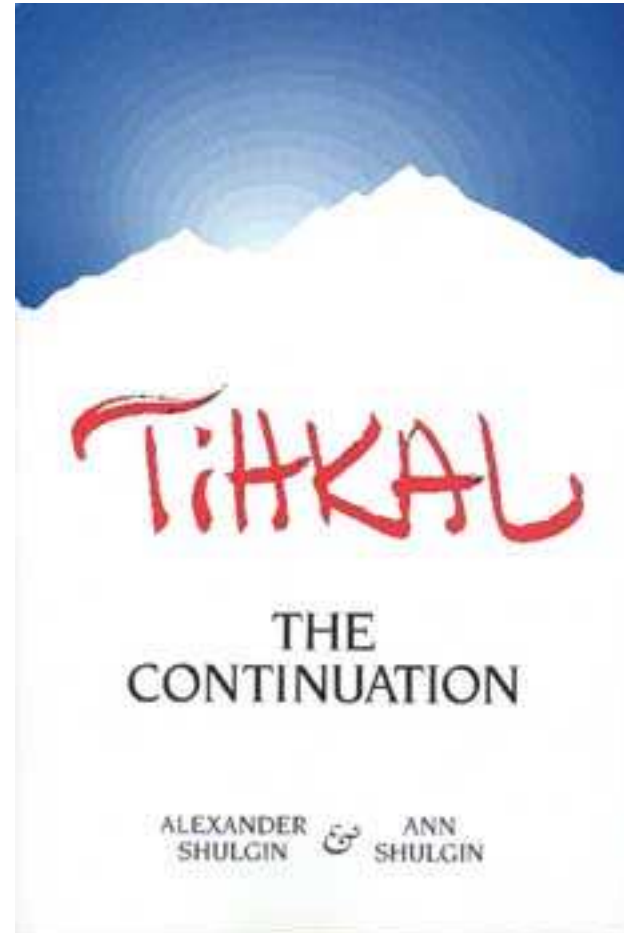
| Effects of 2C-B | |
|-----------------|-----------------|
| Stage | Time |
| Onset | 20 - 90 minutes |
| Coming up | 15 - 30 minutes |
| Plateau | 2 - 3 hours |
| Coming down | 2 hours |
| Aftereffects | 2 - 4 hours |

PKD in the early 1970s

-His third wife had left him, and his Northern California home had become a crash pad and commune for junkies and runaways. His fragile sanity fared no better than his relationships, and he became buried in his own paranoia, hiring hit men to protect his drug-addicted friends and becoming convinced that the FBI was watching his every move. He *began experimenting with a variety of pills...*

Tryptamines

- Tryptamines I Have Known And Loved
- 1997
- Indole-group



DMT-like drugs

- ❑ Schedules of controlled substances: placement of alpha-methyltryptamine (AMT) and 5-methoxy-N,N-diisopropyltryptamine (5-MeO-DIPT) into schedule I of the Controlled Substances Act (Sept 2004)
- ❑ One 4th-position tryptamine that deserves consideration and investigation is the N,N-diethyl cousin of psilocin/psilocybin called 4-hydroxy-DET (see entry #16 in *TIHKAL*) or more commonly referred to as **CZ-74** in the scientific literature.

Newest designer drugs

- ❑ of the new benzyl or phenyl piperazine type (eg, BZP, MDBP, mCPP, TFMPP, MeOPP)
- ❑ of the pyrrolidinophenone type (eg, PPP, MOPPP, MDPPP, MPPP, MPHP) have gained popularity and notoriety as rave drugs.
- ❑ these drugs produce feelings of euphoria and energy and a desire to socialize.
- ❑ knowledge of the metabolism is a prerequisite for toxicologic risk assessment. Polymorphically expressed CYP2D6 is the major enzyme catalyzing the major metabolic steps of the studied piperazine- and pyrrolidinophenone-derived designer drugs.

Going backward in the future: the ecological drugs

- ❑ Literally hundreds of products are available.
- ❑ morphine and cocaine: earliest examples of the transition of plant to manufactured medicine.
- ❑ Khat illustrates how a lack of technological innovation can impede the wider diffusion of a substance.

Psychonauts' suggested combinations of psychedelics

- `.....Similar to combining **DMT/DPT/5-MeO-DMT with ketamine**, combining **4-acetoxy-DET with ketamine** also provides an incredible synergy. Highly recommended for the **cosmic-mystical near-death inclined!..... Xenon gas while on mushrooms or LSD** comes in at a close second. `

Internet and drugs considerations

(Schifano et al, J Psychopharmacology, November 2005; Schifano et al, Progr Neuropsychopharmacol Biol Psychiatry, Feb 2006)

- ❑ The Internet offers the best and quickest way to realise any exchange of news, trends and money and its popularity is especially on the increase in the "dot-com" generation
- ❑ Those who meet the prerequisites of literacy, Internet access and credit card ownership and who are most likely to come from the socio-economically privileged sections of society may possibly comprise the group of "expert drug users"/"psychonauts"

The Psychonaut Early Warning System project

- ❑ An exhaustive web mapping on drug-related issues can provide significant and updated information on new drugs, new trends and modification of drug scenarios
- ❑ The web might be of huge interest for the practising clinician

The Psychonaut Early Warning System project

1st step

- monitoring of the web and identification of putative novel misusing compounds/novel combinations
- online queries will be formulated, with the help of search engines and scanning softwares, with a selection of different keywords. To carry out further Psychonaut EWS exercises on selected compounds, a purposeful website sampling technique will be used.

The Psychonaut Early Warning System project;

2nd step

- ❑ Once a putative novel psychoactive compound/combination of compounds will be identified, the scientific literature will be first thoroughly searched
- ❑ When related law enforcement data (i.e.: seizures; deaths; arrests for possession; drug related offences) will not be available at all, a few 'key informants' (clinicians involved in the Psychonaut EWS network; ravers; club attenders; Community Drug Treatment clients; web surveys respondents etc) will be approached.
- ❑ Key informants will act as 'sentinel networks'
- ❑ Finally, a clinical pharmacological/toxicological risk assessment for each identified compound will be carried out.

The Psychonaut Early Warning System project;

3rd step

- the processed information will be posted on the Psychonaut EWS website
- access will be restricted to identified health agencies: A&E departments; Drug Treatment Centres; National Poison Centres.

Polypharmacy use

- ❑ alcohol is taken with ecstasy at the beginning of the night to get a stronger/better high (MDMA, whilst in the presence of alcohol, shows more significant physiopathological effects. Other options: pre-party packages containing SSRIs; moclobemide
- ❑ Cocaine, amphetamines and/or additional ecstasy tablets are taken to maintain arousal and a state of alertness (the MDMA entactogenic effects fade away in 2 – 4 hours).
- ❑ Finally, opiates and/or high (i.e. sedatives) dosages of alcohol are taken in the last part of the night to calm down before going home since the untoward after-effects of ecstasy (namely: irritability and restlessness) persist well beyond the end of the empathogenic and entactogenic pleasurable effects.

Conclusions (1)

- ❑ Illicit drugs' pharmacodynamics is very complex; too many gaps in knowledge. Different brain structures and different neurotransmitters are involved in the different stages of the addiction process
- ❑ Psychoactive effects may be highly rewarding; with a 100% bioavailability (ie: crack cocaine) addictive liability characteristics reach the highest levels known for a drug

Conclusions (2)

- ❑ Take into account the bio-psychosocial model; role of Narcotics Anonymous et similia
- ❑ In the long run, the psychopathological consequences are the norm, and NOT the exception