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# MESSAGE FROM THE SECRETARIAT

ATUL AMBEKAR  
SECRETARY GENERAL, APSI

Dear readers

Greetings from the secretariat of the Addiction Psychiatry Society of India (APSI). Your society, APSI, is just a three-year young organization which has already registered an impressive growth in a short span of time.

Providing a vibrant platform to its members for achieving excellence in training, research and clinical care is the core vision of APSI. Towards this end, we conduct several activities such as annual conferences as well as CMEs. However, a need was felt by the membership for a vehicle of communication with the members on a periodic basis. We bowed down to your wishes and started planning the publication of a digital periodical. The result of the hard work by the editorial team is in your hands on your screens, the newsletter **"APSI NEWSBUZZ."**

Moving with the times, it has been a conscious decision to produce this newsletter only in the digital (pdf) format. The editorial team has deliberately avoided making the newsletter too 'academic' (read: dry or boring). However, the attempt will be to introduce the readers to one or the other special, focused facet of Addiction Psychiatry as well as keeping the readers abreast of the activities of APSI. We hope you find it interesting, engaging and thought-provoking. As I envision it, eventually, APSI will make progress towards producing a scientific journal of its own. Till then, this newsletter will be one of our many channels of communication.

Enjoy reading this inaugural issue. Do let the editorial team know of your thoughts and ideas for future issues. Lastly, if you have not joined APSI yet, avoid the FOMO! Join us today on <https://addictionpsychiatry.in/membership-application/> and be a part of the movement towards growth of addiction psychiatry in India.

Yours in solidarity  
Atul Ambekar

# FROM THE EDITORS' DESK

## MEDICAL CANNABIS USE : THE CONSIDERATIONS

RAVINDRA RAO, PREETHY KATHIRESAN  
AIIMS, NEW DELHI

पञ्च राज्यानि वीरुधां, सोमश्रेष्ठानि ब्रूमः |  
दर्भो भङ्गो यवः, सहस्ते नो मुञ्चन्त्वंहसः ||

The use of Cannabis in India has been well-known since ancient times. Bhang derived from cannabis leaves plays a significant role in the religious practices in India, especially during Shivratri, Holi, Kali Puja, and Krishna Ashtami. Smoking of cannabis weed, 'ganja' has also been associated with spirituality and is smoked by Saadhus, sometimes attributed to Lord Shiva himself. Apart from socially sanctioned use, cannabis has also been used for medicinal purpose since ancient times. The earliest mention about Cannabis preparation "Bhanga" can be found in Atharva Veda (2000 BC to 1400 BC) (1, 2). In this scripture,

**...CANNABIS HAS BEEN DESCRIBED  
AS ONE OF THE FIVE MOST  
SACRED GRASSES.**

Furthermore, Sushruta Samhita (600 AD) has described the use of derivatives of cannabis for various ailments. Cannabis has been described to have anti-phlegmatic properties and pain-relieving properties. It has also been used as anaesthetic in combination with alcohol by ancient Indian surgeons. Bhang has also been used as a home remedy for various minor health issues including decreased appetite or digestion problems (3).

Around 1800s, cannabis cultivation expanded in India under British rule, predominantly as a cash crop, for hemp. However, this also led to an increase in the use of cannabis among the general population.

**THIS LED TO THE FORMATION OF THE INDIAN HEMP DRUGS COMMISSION,  
WHICH SYSTEMATICALLY STUDIED CANNABIS USE IN INDIA AND FOUND  
THAT MODERATE USE WAS NOT ASSOCIATED WITH PHYSICAL, MENTAL, OR  
MORAL EFFECTS.**

Cannabis use continued without restrictions in India till the enactment of the Narcotic Drugs and Psychotropics Substances Act (NDPS) in 1985. As India was a signatory to the 1961 and 1971 UN Conventions on Narcotics and Psychotropics, it was mandated to eradicate the "non-medical" use of cannabis. NDPS act was enacted to prohibit cannabis use, except for medicinal or scientific purposes. However, Bhang was kept out of purview of NDPS Act, possibly considering its social and medicinal use. This sudden enactment and enforcement of the law



abruptly criminalised cannabis use and led to an increase in the arrest of many low-level drug users. Around the same time, there was also an increase in use of 'harder' drugs like "heroin" and use of riskier methods of consumption like injection drug use(4).

The enactment of narcotic laws in India and elsewhere led to individuals being imprisoned for use and for possession of cannabis. Additionally, scientific advancement led to cannabis extracts being used for medical conditions, and research evidence for use of these cannabis products, including for cannabis smoking, started accumulating. In some countries, notably in the United States of America (USA), many states made medical marijuana legal or enacted laws decriminalising cannabis use.

## **SOME COUNTRIES (EX: PORTUGAL) HAD EXPERIENCED POSITIVE RESULTS WITH DECRIMINALISATION OF DRUG USE.**

Countries such as Peru, Germany, and New Zealand have legalised cannabis for medical purposes, while countries such as Canada, Uruguay, and Malta have legalised recreational cannabis use (5). Closer home, Thailand has become the first Asian Country to decriminalise Cannabis use. In India, the use of cannabis for medicine or for recreational purpose is governed by the NDPS act. However, there is confusion with respect to the various provisions in the law that needs to be understood when debating about this issue in India. The write-up titled "[Medical Cannabis in India: Legal Implications](#)" by Ms Tripti Tandon, Lawyer and Drug Policy expert, brings out the nuances in the act with respect to the medical use of cannabis.

While legalisation for medical cannabis is gaining more prominence and support from various stakeholders is increasing across the world, there are voices that argue against this move.

## **THE MAJOR ARGUMENT POSED AGAINST THE LEGALISATION OF CANNABIS IS THE FEAR OF INCREASE IN VARIOUS HARMS ASSOCIATED WITH CANNABIS USE...**

...like risk of addiction, cognitive decline, risk of mental illness like psychosis, etc. The implication of these risks with regards to medical cannabis use has been discussed in the write up titled "[Medical Cannabis Use: Will It Increase Mental Health Burden?](#)" by Drs Ghosh and Mishra from PGI, Chandigarh. Much of the conundrum revolving around medical and recreational use of cannabis is also to do with the hundreds of chemicals in the cannabis plant and the complexity of the endocannabinoid system.

## **RESEARCH HAVE IMPLICATED THE ROLE OF CANNABINOID RECEPTORS IN VARIOUS MEDICAL CONDITIONS...**

...like Parkinson's disease, Alzheimer's disease, etc(6). Also, various products derived from cannabis and products acting on the Cannabinoid receptors have been developed that has been approved by drug regulatory bodies for use for various medical conditions(7). Some have even argued that cannabis smoking might be more effective than the consumption of individual cannabinoid products itself (8). The neurobiological underpinning of cannabis use is discussed in the write-up titled "[Delineating medical and non-medical use of cannabis: what does neurobiology inform us?](#)" by Dr Malay Dave,



consultant psychiatrist from Mumbai. While some countries have legalised cannabis use for medicinal purposes, there are also arguments that medical cannabis may be a trojan horse for legalisation of cannabis for recreational purpose. Recently, discussions have started around decriminalisation of cannabis use in India as well (9).

## **INDIA IS IN A UNIQUE SITUATION THAT ITS USE FOR RELIGIOUS AND MEDICAL PURPOSES HAVE BEEN WELL-KNOWN SINCE THE ANCIENT TIMES.**

Some of the cannabis derivatives are also used widely in Ayurveda for medical purposes. Recently, various entities have started selling products containing cannabis leaves and seeds for medicinal purpose and for improving wellness in individuals. It would be interesting to know how does the cannabis industry view medical use of cannabis. The write-up titled "[Potential of therapeutic cannabis use in India: Industry viewpoint](#)" by BoHeCo, one of the Hemp manufacturers in India, provides this perspective.

We hope that our attempt to bring out different aspects of medical cannabis use will stimulate further discussions and reflections on this important area.



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# MEDICAL CANNABIS IN INDIA: LEGAL IMPLICATIONS

TRIPTI TANDON

LAWYER AND DRUG POLICY ANALYST

The medical cannabis debate is catching up in India, though cannabis has been used for therapeutic purposes for centuries.

## MEDICAL USE OF CANNABIS IS PERMITTED

Cannabis is a 'narcotic drug' under the Narcotic Drugs and Psychotropic Substances Act, 1985 ("NDPS Act"), which is modelled on International Drug Conventions including the Single Convention on Narcotic Drugs, 1961, which sanctions the medical and scientific use of such drugs within a framework of prohibition. On the same lines, section 8 of the NDPS Act, while prohibiting drug-related activities, allows the cultivation of the cannabis plant as well as its production, manufacture, possession, sale, purchase, transport, warehousing, use and consumption for medical and scientific purposes. Such operations, however, must be in accordance with Rules or Orders issued under the Act and if such Rules require obtaining a license, then also in accordance with the terms and conditions of such license. The 2014 amendments to the Act included a revision of section 4 by which "ensuring availability of narcotic drugs and psychotropic substances for medical and scientific use" was made an equally important task to be undertaken by the Central Government as 'preventing and combating their abuse'.



**THE NDPS ACT AS IT STANDS TODAY, PERMITS THE MEDICAL USE OF CANNABIS. DEMANDS FOR 'LEGALISING MEDICAL CANNABIS' ARE MISCONSTRUED.**

## ADVOCACY MUST BE DIRECTED AT STATES

Under section 10 of the NDPS Act,...

**...THE POWER TO MAKE RULES TO 'PERMIT AND REGULATE' ACTIVITIES IN RELATION TO CANNABIS RESTS WITH STATE GOVERNMENTS.**

Accordingly, policies for medical cannabis need to be considered at the State-level and advocacy for enabling access directed at State authorities. The Central Government's role is that of encouraging the States to utilise these provisions, as they did in August 2019, when the Director, Narcotics Control in the Finance Ministry's Department of Revenue (which oversees the NDPS Act), wrote to State Governments to facilitate research by the Council for Scientific and Industrial Research (CSIR) on different strains of the cannabis plant in light of the powers conferred on them under section 10 of the NDPS Act. Since drug control is a contentious issue

– legally and politically, States may hesitate to exercise their regulatory authority, even for health objectives, without the nod of Central agencies.

## **SOME GREY AREAS IN LAW**

### **WHAT IS 'MEDICAL CANNABIS'?**

Legally, one of the grey areas is the identity and composition of the substance that can be dispensed as 'medical cannabis.' This is because the...

### **...NDPS ACT CONTAINS NOT ONE BUT MULTIPLE DESCRIPTIONS OF 'CANNABIS,' WHICH ARE SUBJECT TO DIFFERENT PUNITIVE AND REGULATORY MEASURES.**

Under the Act, cannabis can refer to the 'cannabis plant' or 'cannabis hemp' – which is further classified into – i) 'charas' or 'hashish,' commonly known as 'resin' extracted from the plant; ii) 'ganja' which is the flowering and fruiting tops of the plant excluding seeds and leaves when unaccompanied by the tops and, iii) any mixture of charas and ganja including drink. Since seeds and leaves of the plant are excluded from the definition of 'cannabis hemp,' bhang – a preparation made of cannabis leaves is not covered under the NDPS Act.

Another category of cannabis under the NDPS Act is 'medicinal cannabis,' which is defined as 'extracts or tinctures of cannabis hemp.'

### **MEDICINAL CANNABIS IS CLASSIFIED AS A 'MANUFACTURED DRUG' – A CATEGORY THAT ALSO INCLUDES MORPHINE, HEROIN, AND COCAINE.**

While unauthorised activities in relation to the 'cannabis plant' and 'cannabis hemp' i.e., ganja and charas attract penalties under section 20 of the NDPS Act, any contravention for 'medicinal cannabis' is punishable under section 21. Further, 'Tetrahydrocannabinol' ('THC'), which is a compound found in the cannabis plant and provides the intoxicant effect, is notified as a 'psychotropic substance,' for which punishment is prescribed under section 22 of the Act. Though treated differently in law, there is some overlap between these substances. For e.g., 'medicines containing bhang' should be out of the purview of the NDPS Act since the source, i.e., bhang is itself excluded. However...

### **...IN SOME CASES, ENFORCEMENT AGENCIES HAVE PROSECUTED BHANG-BASED PRODUCTS AS THEY CONTAIN 'THC' – A PSYCHOTROPIC SUBSTANCE.**

The identity and composition of cannabis medicine is also important for legal regulation. Some State NDPS Rules authorise the Government to license cultivation of the cannabis plant for medical and scientific purposes. These clauses are 'enabling' in nature and allow the authorities to determine, by general or special order, the type and variety of cannabis plants that can be grown in the State, such as strains with low THC.

### **A FEW STATES PERMIT MEDICAL PRACTITIONERS TO POSSESS GANJA AS AN 'INGREDIENT FOR ANY MEDICINE' AND TO SELL 'MEDICINES CONTAINING GANJA' AFTER OBTAINING A LICENSE ('NDPSL').**

The ganja must be procured from a Govt-established depot, which must further source it from a Govt-warehouse or any other place directed by the Excise Commissioner. As far as charas and hashish-based products are concerned, no State can allow cannabis-resin for medical use.

Interestingly, all states have Rules permitting the use of 'medicinal cannabis' as a 'manufactured drug,' even though the DCGI/CDCSO do not recognise 'cannabis' as a drug for allopathic treatment.

## **PRACTITIONERS OF 'AYURVEDA,' 'SIDHA,' AND 'UNNANI' SYSTEMS OF MEDICINE ARE, HOWEVER, AUTHORIZED TO USE BHANG AND GANJA IN THEIR PRACTICE.**

Not much is known about the actual implementation of the State NDPS Rules and the dispensing systems, if any, for 'medicinal cannabis.'

### **WHAT IS 'MEDICAL USE'?**

Another ambiguity for 'Medical cannabis' is that...

#### **...'MEDICAL USE' IS NOT DEFINED IN LAW.**

It is generally understood in reference to the 'prevention, diagnosis, treatment, cure, management or mitigation of disease.' Should the use of cannabis be considered 'medical' only if it is under the supervision or prescription of a doctor? What about self-medication? Some of the 'medical cannabis' available online are described as 'ayurvedic' or 'herbal' preparations or as 'wellness' products. Anyone can purchase them. It is also unclear whether the suppliers comply with the pharmacological and legal standards applicable to medicines and medical commodities.

To conclude, while medical cannabis is legal in India, the legal implications associated with its use are unpredictable. Norms around the substance and what qualifies as its medical use need to be set. Without this, doctors and patients will remain in the shadow of the draconian NDPS Act, as they have been in relation to other opioid medicines.

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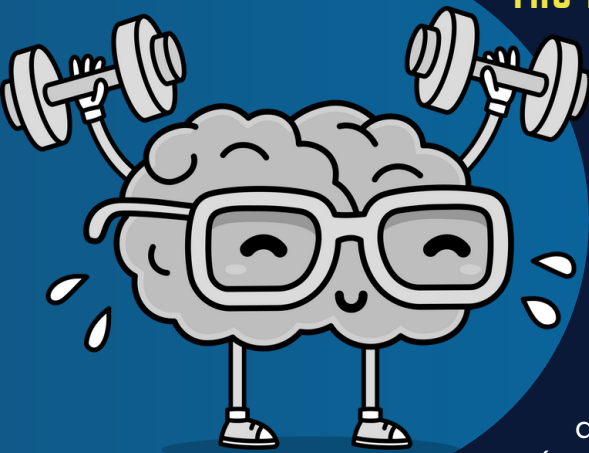
# MEDICAL CANNABIS USE : WILL IT INCREASE MENTAL HEALTH BURDEN?

ABHISHEK GHOSH, EEPSITA MISHRA

PGIMER, CHANDIGARH

## TYPES OF CANNABIS USE – MEDICAL VS. MEDICINAL

'**Medical use**' of cannabis refers to using a cannabis-based product for medical purposes, for example, Dronabinol for chemotherapy-related nausea. Only a few medications are approved to treat a limited number of medical conditions. A related term is 'medicinal use,' which describes the beneficial effects of a drug or herb (1). Medicinal use is broader and encompasses most of the so-called medical use of cannabis. Despite the technical differences between these two terms, for this write-up, we will use medical cannabis to refer to any non-recreational or therapeutic cannabis use. Cannabis herb or naturally occurring cannabis contains more than 550 chemical compounds- more than 100 Phyto cannabinoids, including tetrahydrocannabinol (THC) and cannabidiol (CBD). Cannabinoids have additive, synergistic, or antagonistic effects, and THC is the chief psychoactive compound (2).



**THC IS IMPLICATED IN CANNABIS-ASSOCIATED HARMS, SUCH AS PSYCHOSIS. CBD, AN ANTAGONIST TO THC, MIGHT REDUCE THIS RISK. THEREFORE, THE THC:CBD RATIO COULD INFLUENCE THE HARMS VERSUS BENEFITS OF MEDICINAL CANNABIS USE.**

However, the concentrations of THC, CBD, and other compounds vary widely according to different sources and agricultural practices. Moreover, the mode of use (dabbing vs. vaping vs. smoking vs. oral ingestion) also affects the amount of THC that reaches the bloodstream.

Consequently, several cannabis and "user"- related variables might influence harm due to medicinal cannabis use. So, medical cannabis is not a standardized and uniform product (as opposed to standard medicines, e.g., paracetamol); hence, harm caused by or associated with it might be unpredictable and even unknown. In this write-up, we will specifically focus on the mental health effects of medical cannabis- beneficial (as treatment) vs. harmful effects.

## EVIDENCE OF MEDICAL CANNABIS IN MENTAL ILLNESS

No regulatory bodies have approved medical cannabis for any mental illness. Nevertheless, systematic reviews of controlled and observational studies showed potential positive effects of cannabis on anxiety, anorexia nervosa, post-traumatic stress disorder (PTSD), psychosis, and agitation in dementia. There might be a small but significant effect of medical THC on



anxiety symptoms in patients with chronic pain and medical illness (3). However, the evidence is inconsistent, and the lack of robust methodology and the consequent high risk of bias have dampened the interest in medical cannabis use for mental illness (4).

Moreover, medical cannabis use is associated with greater rates of depression, cognitive impairments, accidents, and acute care utilization, especially among elderly persons (5).

Medical cannabis also increases any adverse events and withdrawals due to adverse events (3). The cognitive impairment in adults might be transient. Medical cannabis use is not seen to be associated with the risk of self-harm and is rarely associated with serious adverse events (6). Overall, . . .



### **...THE HARM SEEMS TO OUTWEIGH THE BENEFITS OF MEDICAL CANNABIS USE FOR MENTAL ILLNESS, SPECIFICALLY AMONG OLDER ADULTS.**

Despite the lack of evidence, around half of all medical cannabis users report anxiety as a reason for using medical cannabis and around a third of patients endorse medical cannabis use for depression (7).

### **WHAT ARE THE MENTAL HEALTH EFFECTS OF CANNABIS USE?**

Medical cannabis use may lead to problematic use of cannabis and other substances. However, contradicting evidence suggests using cannabis as an 'exit drug' as a harm reduction strategy in opioid and alcohol dependence treatment. Recent studies revealed increased risks of motor vehicle accidents and emergency room admissions in medical cannabis users. Both anxiogenic and anxiolytic roles have been described in the context of cannabis – the former as part of cannabis withdrawal syndrome and the latter contributing to its role in Social Anxiety Disorder and PTSD. While several users cite elevation of mood as a reason for use, non-medical use of cannabis is associated with an increased risk of depression (4,5).

### **PRECIPITATION OF PSYCHOSIS REMAINS THE MOST SERIOUS ADVERSE EFFECT OF CANNABIS USE; LONG-TERM USE, ESPECIALLY EARLY-ONSET USE, IS ASSOCIATED WITH NEUROCOGNITIVE DECLINE.**

#### **BLURRING OF LINES BETWEEN MEDICINAL AND RECREATIONAL CANNABIS USE**

Due to loosely regulated supply, production, and access, at times, boundaries between medically sanctioned cannabis use and non-medical or recreational use can easily become blurred. Patient's reasons for using medical cannabis may differ from the actual degree of benefit experienced and the original reasons for prescription. The legal status of medical cannabis may influence the patient-reported reasons for use and may not necessarily be an accurate reflection of the actual reasons for use (3). With prolonged use, there is a risk of medical use devolving into recreational use and eventual problematic use or dependence. Heavy and prolonged recreational use of cannabis has been linked with increased risk of suicide, psychosis, depression, cardiovascular morbidity and roadside accidents (6).

## MEDICAL CANNABIS AND MENTAL HEALTH BURDEN

Whether or not legalization of medical cannabis use would increase the mental health burden is a complex question. Observational studies from the US showed that the passage of medical cannabis laws is associated with increased cannabis use and use disorder (CUD). However, young, non-white men with concurrent mental illness and a history of substance use disorder are more likely to develop CUD (8, 9). Among those on authorized medical cannabis use, the hospitalization and emergency visit rates due to mental illness were 15 per 10,000 person-years. Again, concurrent mental illness, other SUD, and medical illness increased the risk of hospitalization (10). With observational studies, causal inferences cannot be made. Moreover, these studies were from North America, and the association must be investigated from other countries. Nevertheless, ...

**...A CONSISTENT ASSOCIATION OF CUD AND MEDICAL CANNABIS IS A REASON FOR CONCERN. AS DISCUSSED, THE DIFFERENCE BETWEEN MEDICAL AND RECREATIONAL USE IS OFTEN BLURRED, AND THE LATTER USE, ESPECIALLY HEAVY USE, INCREASES THE RISK OF MENTAL ILLNESS.**

Decreased risk perception and normalization of cannabis use due to the approval of medical cannabis may increase adolescent use. Use of cannabis at an early age has higher cognitive and mental health adverse effects. Finally, inappropriate medical cannabis use for mental illness could lead to delays in evidence-based treatment and consequent harm. Overall, the direct and indirect evidence suggests that medical cannabis use may increase the mental health burden at the population level.

## CONCLUSIONS

Cannabis is a powerful psychoactive substance with varied psychological and physical effects.

**THESE EFFECTS CAN SOMETIMES BE PARADOXICAL AND CONTRADICTORY DUE TO THE DELICATE BALANCE BETWEEN HUNDREDS OF ALKALOIDS – THE COMPOSITION OF WHICH IS UNIQUE AND UNPREDICTABLE IN NATURALLY CULTIVATED CANNABIS.**

Available evidence points to cannabis as a potential therapeutic option for some mental health conditions– however, considering simultaneous contradicting evidence, these results need to be replicated in good-quality studies. Legislative policies making cannabis of varying potency and composition freely available to citizens, even for medicinal purposes, is premature and may lead to an increased mental health burden. However, countries must increase the access and availability of medicinal cannabis to conduct ethical and robust experimental research. An evidence-informed and public-health-oriented policy should replace the current idiosyncratic and market-influenced policies.



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# DELINEATING MEDICAL AND NON-MEDICAL USE OF CANNABIS: WHAT DOES NEUROBIOLOGY INFORM US?

MALAY DAVE

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## INTRODUCTION

Cannabis sativa is widely cultivated all over the world for its fiber and its psychoactive component (ganja, marijuana, bhang, pot, etc) (1).

## DELTA-9-TETRAHYDROCANNABINOL (THC) PRODUCES THE EUPHORIANT EFFECTS, WHILE CANNABIDIOL (CBD) HAS THERAPEUTIC POTENTIAL IN SEVERAL DISORDERS.

THC is relatively specific for cannabinoid receptors, and CBD modulates the activity of several proteins. Apart from THC & CBD, more than 100 cannabinoids have been identified, and almost all are non-psychoactive (2). Cannabis products can be used through a variety of routes. Oral ingestion of raw plant material, smoking, vaping, dabbing, sublingual (tinctures & oils), edibles (gummy candies, truffles, and the more traditional cookies, brownies, and sauces) and rectal (1, 2).



## NEUROBIOLOGY

The endocannabinoid system in the human body and brain mediates the effects of exogenous THC & CBD. Endogenous compounds, viz. anandamide and 2-arachidonoylglycerol are the primary agonists. Other agonists include N-arachidonoyldopamine (NADA), 2-arachidonoylglycerylether (noladin ether), O-arachidonylethanolamine (virodhamine). Congeners which exert their effect independent of the cannabinoid receptors are N-palmitoylethanolamine (PEA), N-oleoylethanolamine (OEA), and N-stearoylethanolamine(3). The main receptors of the endocannabinoid system are CB1R & CB2R. Both are G-protein Coupled Receptors (2, 4).

## CB1R ARE LOCATED PRESYNAPTICALLY IN EXCITATORY AND INHIBITORY NEURONS, ASTROCYTES, AND IN THE EXTERNAL MEMBRANES OF MITOCHONDRIA, ENDOSOMES & LYSOSOMES.

CB1R is also present in the liver, reproductive system (testes & ovaries), GIT, CVS, and Skeletal muscles (4). These receptors mediate short-term and long-term forms of synaptic plasticity, long-term depression, and long-term potentiation, slow self-inhibition of neocortical interneurons, and change expression of precursors of appetite-controlling peptides in the arcuate nucleus of the hypothalamus, leptin signaling in the hypothalamus, pain modulation, bone remodeling, cancers, and stimulate proliferation of adult progenitor stem cells and their differentiation into neurons or astrocytes (2, 4).

## **CB2R PLAY A ROLE IN IMMUNE MODULATION.**

These are expressed at very low levels in healthy neurons and their activation has the opposite effects to CB1 activation(2).

N-acylphosphatidylethanolamine (NAPE)-specific phospholipase d-like hydrolase (NAPE-PLD), Fatty acid amide hydrolase (FAAH), Diacylglycerol lipase  $\alpha$  (DAGL $\alpha$ ) and DAGL $\beta$ , Monoacylglycerol lipase (MAGL) are the major enzymes involved in the metabolism of endocannabinoids(2). However, the endocannabinoid system is much more complicated than this. There are many mediators and a significant overlap with other pathways. This complete network is known as the endocannabinoidome. The complexity of the endocannabinoidome is seen in the following (2):

- Enzymes for endocannabinoid degradation also degrade other substrates – for example, FAAH also degrades peroxisome proliferator-activated receptor- $\alpha$  (PPAR $\alpha$ )
- Endocannabinoid biosynthesis – eg. Anandamide and 2-AG can be produced by several pathways.
- There are multiple targets for the endocannabinoids – for example, anandamide activates TRPV1 and PPAR $\gamma$  receptors apart from CB1 & CB2R.
- There are many endocannabinoid-like mediators – for example, N-acyl-aurines, N-acyl-serotonins, N-acyl-dopamines, fatty acid primary amides and a plethora of N-acyl-amino acids.
- There are allosteric modulators of CB1 and CB2 – for example, haemopressins and related peptides.
- Other endocannabinoidome receptors have also been discovered – for example, TRPV1 (Transient Receptor Potential Cation Channel Subfamily V Member 1)
- The endocannabinoidome and gut microbiota have complex interplay and interactions.

The various components of the endocannabinoid system are genetically controlled. Eg. FAAH gene on chromosome 4. Epigenetic control of the enzymes, receptors & other molecules of the endocannabinoidome is also being actively studied. (3)

## **MEDICAL USES**

The complexity of the endocannabinoid system provides multiple targets for various neurological and psychiatric illnesses.

## **MULTIPLE COMPONENTS OF THIS SYSTEM ARE INVOLVED IN THE PATHOGENESIS OF VARIOUS DISORDERS.**

For example, in Parkinson's Disease, Biphasic dysregulation of CB1R (hypoactivity in pre-symptomatic and early PD and hyperactivity at later stages), CB2R upregulation, and increased Endocannabinoid levels have been documented. Accordingly, CBD, THC, and Nabilone have been tried in various trials(2).

## **SIMILARLY, CBD HAS BEEN TESTED IN ALZHEIMER'S DISEASE PATIENTS FOR PROTECTION AGAINST A $\beta$ -INDUCED INSULTS.**

Nabilone, Nabiximols, and Palmitoylethanolamide have been trialed for use in Huntington's Disease, AML, Multiple Sclerosis, Glioblastoma, and Stroke. Dexamabinol, an



enantiomer of the ultra-potent synthetic CB1 and CB2 ligand HU-210, has exhibited potent neuroprotective activity in patients with traumatic brain injury (TBI). CBD has shown promise in management of seizures in Dravet syndrome and Lennox-Gastaut syndrome, and treatment-resistant epilepsy (2). Cannabis products like Dronabinol have been found to be useful in the treatment of appetite disturbances & nausea in cancer and HIV patients and sleep apnea.

Like in neurological disorders, dysfunction & abnormalities in the endocannabinoid system have been discovered in Schizophrenia (increased CB1R density), where Rimonabant, CBD, PPAR- $\alpha$  targets have been found to be useful. Similarly, involvement of the endocannabinoid system in anxiety, mood disorders, & addictions is an active area of research in understanding newer therapeutic targets (2). The psychoactivity of THC narrows its therapeutic window and limits its applications, but..

## ...CBD IS MORE AMENABLE TO CLINICAL DEVELOPMENT.

### NON-MEDICAL USE

While the medical uses of cannabis are being explored, there are growing health concerns associated with non-medical use of cannabis. Recreational or regular use of cannabis in a genetically susceptible individual increases the risk of psychiatric illnesses, including Cannabis Use Disorder. Studies of effects of cannabis in utero and perinatal exposure have broadened our understanding of the developmental effects of cannabis (5). More potent forms of cannabis products are available nowadays (increase in the percentage of THC and increased ratios of THC to CBD), which can have more deleterious effects on the brain and body function(5).

### CONCLUSIONS

Cannabis and its products are unique in many ways. There are multiple chemicals present in the cannabis plant; the role of some has been delineated, while the role of others is still being explored. Similarly, these chemicals also have effects that are opposite of each other. The endocannabinoids not only have primary action on cannabinoid receptors but also modulate various other pathways that have a role in various neuro-psychiatric illnesses. The medical uses of cannabis and cannabis products are still being explored and evidence present are preliminary at this stage. More evidence is required before these products can be approved and used clinically.

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# POTENTIAL OF THERAPEUTIC CANNABIS USE IN INDIA: INDUSTRY PERSPECTIVE

JAHAN PESTON JAMAS, NEERAJ KUMAR PATEL, HARSHAD JAIN

BOHECO, MUMBAI

## INTRODUCTION

The Medical Cannabis industry encompasses cannabinoid-based medications, that are provided through the healthcare system and recommended by a doctor with the primary goal of reducing serious disease symptoms. Medical Cannabis, also known as medical marijuana, describes the medicines derived from plants' leaves (Bhaang) and flowers (Ganja) globally. The products made from medical cannabis have therapeutic uses and are designed to enhance the quality of life, such as elevating mood, improving sleep quality, reducing pain, improving appetite, and lowering stress and/or anxiety. Globally, the maturity of the cannabis market varies, primarily because of various legal frameworks and societal perceptions of cannabis. Some nations, including Canada, the US, Israel, Australia, and Germany, have fully regulated frameworks in place that permit the production, use, and retail sale of various cannabis products. Regulations around cannabis' use for medical/therapeutic purposes use can also vary from region to region. Tetrahydrocannabinol (THC)-rich products can be consumed in some countries, but only for medical purposes. Whereas in most countries, CBD based Cannabis medicines have already been approved and are actively being prescribed by practitioners for a range of indication areas.



**IN INDIA, THE MEDICINES MADE FROM THE LEAVES (BHAANG) OF THE CANNABIS PLANT ARE USED FOR THERAPEUTIC PURPOSES. THE PRODUCTS INCLUDE BOTH PRESCRIBED (INGESTIBLE) AND OVER-THE-COUNTER MEDICINES (TOPICALS) THAT CAN BE TAKEN AS OILS, PILLS, CREAMS, SPRAYS, ETC.**

Cannabis has a long history of use in India, dating back thousands of years. It is mentioned as "Vijaya" in ancient Indian texts, including the Atharva Veda, one of India's oldest sacred scriptures. Cannabis was used for both medicinal and ritualistic purposes in ancient India. Cannabis (Vijaya) is considered one of the "Five Sacred Plants" in Ayurveda, along with Tulsi (Holy Basil), Ginger, Turmeric, and Amla (Indian Gooseberry).

**AYURVEDA RECOGNIZES VARIOUS PROPERTIES OF CANNABIS, INCLUDING ITS POTENTIAL AS AN ANALGESIC, ANTI-INFLAMMATORY, AND SEDATIVE.**

In Ayurveda, cannabis is believed to have therapeutic benefits for certain conditions. Some of the potential therapeutic benefits include pain relief from chronic pain and neuropathic pain, helping reduce anxiety and stress, appetite stimulants, improving sleep quality, and managing insomnia.

As a pioneering company within the Indian Hemp & Cannabis space, BOMBAY HEMP COMPANY PRIVATE LIMITED (BOHECO), in line with this requirement, manufactures all products using the Cannabis (Vijaya) seeds and/or the leaves (popularly known as 'Bhang') as ingredients. Therefore, Ayurvedic medicines that contain Bhang and/or Vijaya seeds as an ingredient, are not regulated as narcotic drugs under NDPS Act. Rather,...

**...THE CANNABIS (VIJAYA) LEAF IS REGULATED AS A SCHEDULE E1 INGREDIENT UNDER THE DRUGS & COSMETICS ACT, WHEREAS THE CANNABIS (VIJAYA) SEEDS ARE REGULATED AS A FOOD INGREDIENT UNDER THE FSSAI ACT.**

While it is understood the social stigma attached to the core ingredient of our product, it is important to clarify that such products & medicines are for therapeutic, medical, and nutritional purposes only. Ayurvedic medicines for oral consumption made from 'Bhang' (Cannabis leaves) should always be taken under medical supervision only against a valid prescription issued by a registered medical practitioner.

**AS OF TODAY, 30,000 TO 50,000+ PATIENTS ARE TREATED WITH CANNABIS-BASED MEDICINES IN INDIA...**

...and BOHECO's contribution is close to 20,000 to 25,000 patients which has helped 150+ Ayurvedic and Modern medicine practitioners to generate real-world evidence (Observational/Case basis) to establish the safety and efficacy of Ayurvedic Cannabis-based medicines.

**AT PRESENT, THE DOMESTIC INDIAN MEDICAL CANNABIS AND HEMP INDUSTRY IS ESTIMATED TO BE AROUND INR 80 CR – 110 CR ON AN ANNUAL BASIS, WITH 75+ COMPANIES AND ORGANIZATIONS HAVING ENTERED THE INDUSTRY WITHIN THE LAST 3+ YEARS.**

This number is only expected to exponentially grow, basis the rising demand for & awareness of Cannabis based medicines.

Furthermore, companies such as BOHECO and industry associations such as PIMCHA have been actively engaging the state governments of Uttarakhand, Himachal Pradesh, Madhya Pradesh, Karnataka, Arunachal Pradesh, and several others to assist with the development of robust policies that would legally permit the cultivation of Cannabis in these states (under relevant licenses) for medical, scientific & industrial purposes. To augment these efforts companies such as BOHECO have partnered with CSIR institutes such as CSIR-NBRI to breed botanical varieties of high-quality Cannabis that can provide standard yields to farming communities & industry at the time of commercial cultivation within the aforementioned states. BOHECO is India's first and premier vertically integrated (complete control of supply chain), direct-to-consumer Medical Hemp/Cannabis company, established ten years ago and backed by industry stalwarts such as Mr. Ratan Tata.

BOHECO has been working with Indian union and state governments, local industry, and farmers to reform the agriculture industry and boost Hemp (Cannabis)'s role in the economy, while manufacturing and researching innovative agro-products from the medical hemp (Cannabis) and Industrial Hemp crops for the Ayurvedic Traditional Medicines, Phyto-pharmaceuticals, Foods, Cosmetics industries.

To create a catalytic value chain of clinical data that firmly establishes the safety & efficacy of Cannabis medicines, BOHECO has been the first and only company in India's history to engage a range of medical & academic institutes such as the National Institute of Ayurveda (Jaipur) and Tata Memorial Centre (Mumbai) on human grade safety & efficacy studies with topical + ingestible Ayurvedic Hemp/Cannabis leaf based medicines for multiple indication areas such as Knee based Osteoarthritis, Eczema, Atopic Dermatitis, Stress based Disorders, Sleep based disorders, Irritable Bowel Syndrome, Chronic non-cancer based neuropathic pain and Chronic Cancer based (Palliative) pain.



BOHECO regularly generates clinical evidence, through which the aim is to unlearn the views on cannabis and win the trust of scientific and regulatory communities. Companies such as BOHECO have partnered with the National Institute of Ayurveda, Jaipur, to conduct clinical trials for lifestyle ailments such as arthritis, eczema, digestive issues, stress, and others in the pipeline. Clinical studies have witnessed real impact and improvement of patients' quality of life.

With the rapidly evolving global markets for Medical Cannabis seeing accelerated developments in other Asian countries like Thailand, China & Australia, the era has come for India to leverage the historical & cultural value of Cannabis in Indian society to reassert a position of strength as a growing strategic player within the Global Cannabis & Hemp economy.

*Note: APSI does not endorse or promote any product which may be mentioned or depicted by the authors. Reader's discretion is advised.*

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# RECENT ADVANCES : BASIC SCIENCES

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NIMHANS, BENGALURU

There have been significant advances in our understanding of the neurobiological basis of addictive disorders over the last few decades. In this article, we will highlight a few key studies published in the last two to three years pertaining to basic sciences whose findings are novel and may influence practice.

## UPDATES IN NEUROBIOLOGY OF ADDICTION

The identification of brain regions and networks related to addiction has been a major area of research. A systematic review of whole-brain voxel-based morphometry (VBM) studies by Pando-Naude et al. found...

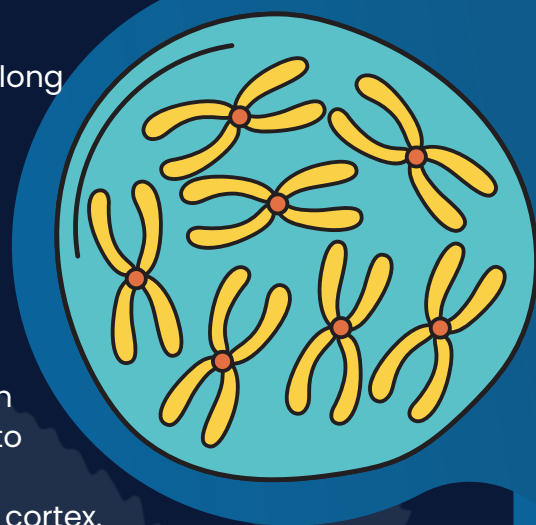
### ...SIGNIFICANT GRAY MATTER CHANGES IN INSULA, ANTERIOR CINGULATE CORTEX, BASAL GANGLIA (PUTAMEN), AND THALAMUS, AND WHITE MATTER CHANGES IN THE THALAMIC RADIATION AND INTERNAL CAPSULE BUNDLE ACROSS SUBSTANCES.

There were also some differential effects for occasional use, long term use and addiction (1). Another interesting study by [Joutsa et al.](#), investigated individuals who were active daily smokers and then attained remission of addiction following an acquired brain lesion. The brain lesions identified in these individuals were then mapped using human connectome data to identify brain regions and networks related to addiction. The study found that although lesions occurred in many different brain locations, they shared a specific pattern of brain connectivity, characterized by positive connectivity to the dorsal cingulate, lateral prefrontal cortex, and insula and negative connectivity to the medial prefrontal and temporal cortex.

This circuit was reproducible across independent lesion cohorts, associated with reduced alcohol addiction risk, and was specific to addiction metrics. The specific brain regions or hubs that best matched the connectivity profile for addiction remission were the paracingulate gyrus (area involved in cognitive and affective regulation), left frontal operculum (part of the frontal lobe covering the insula, and considered to play a key role in response selection), and medial fronto-polar cortex (area involved in cognition, as well as one of the areas targeted in some of the previous rTMS studies related to addiction). These could potentially provide testable targets for therapeutic neuromodulation studies (2).

## UPDATES IN GENETICS OF ADDICTIVE DISORDERS

A better understanding of the genetics of addictive disorders, including the contribution of





general and substance specific factors is another interesting question. This was investigated in a study done by Hatoum et al., using genetic data summary statistics from 1,025,550 individuals of European descent and 92,630 individuals of African descent with problematic alcohol use, problematic tobacco use, cannabis use disorder and opioid use disorder. A total of 19 independent single-nucleotide polymorphisms were genome-wide significant for the general addiction risk factor (addiction-rf).

## **PDE4B WAS ONE OF THE GENES IMPLICATED ACROSS ANCESTRIES, SUGGESTING DOPAMINE REGULATION AS A CROSS-SUBSTANCE VULNERABILITY.**

PDE4 is a cMAP-specific phosphodiesterase that is expressed in several brain regions associated with addiction. Of the various subtypes of PDE4,

## **PDE4B HAS BEEN FOUND TO BE IN ABUNDANCE IN NUCLEUS ACCUMBENS, AN IMPORTANT LOCUS IN ADDICTION.**

PDE4B gene has also been implicated in other mental illness like Schizophrenia and Bipolar affective disorder. Substance-specific loci (9 for alcohol, 32 for tobacco, 5 for cannabis and 1 for opioids) including metabolic and receptor genes, were also identified. These genetic risk loci for substance use disorders could potentially be leveraged as treatment targets, using existing or new drugs (3).

## **GINA MODEL**

The recently proposed GINA (Genetically Informed Neurobiology of Addiction) model (4) attempts to tie some of these findings together and illustrates that...

## **...ALL STAGES OF ADDICTION (BINGE-INTOXICATION, WITHDRAWAL-NEGATIVE AFFECT, AND PREOCCUPATION-CRAVING) ARE INFLUENCED BY A POLYGENIC CORE, ENVIRONMENTAL FACTORS, AND BRAIN SUBSTRATE.**

The polygenic liability lies at the core, with four key domains of genetic risk – genes affecting reward and risk-taking (positive urgency), genes affecting negative affect and/or susceptibility to negative urgency, genes affecting executive functioning/regulation and genes determining drug specific metabolic factors. Genetic vulnerability to risk-taking influences early drug-seeking behaviours. The polygenic liability to deficits in executive functioning in turn modify prefrontal regulatory capacity which ultimately potentiate preoccupation with drugs. Both of these are characteristic of positive urgency, with subsequent changes in striatal circuitry which results in progression through addiction stages. Similarly, negative urgency is characteristic of common inheritance of addictive disorders along with co morbid mood disorders.

The GINA model places environment as the filter through which addiction emerges with specific environmental factors like trauma (especially in early life) having the capacity to alter brain development and ultimately increasing addiction risk in the future.



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# RECENT ADVANCES : ALCOHOL AND TOBACCO

SUKRITI MUKHERJEE, ANIRUDDHA BASU  
AIIMS, KALYANI

## NEWER DRUGS FOR TREATMENT OF ALCOHOL USE DISORDER

### **PRazosin:**

Although (Alcohol Use Disorder) AUD is a common cause of medical morbidity and mortality, there are limited treatment options for treating AUD. Prazosin, a potent antagonist at the postsynaptic alpha-1 receptors, can readily cross the blood-brain barrier and block noradrenergic excitation of the mesolimbic dopaminergic system, as seen in animal models. (1) Recently, it has been found to be effective in reducing adrenergic tone, cutting down alcohol craving and restoration of activity of the medial prefrontal cortex in laboratory animals and patients in a proof-of-concept study. Sinha and colleagues (2023) have explored whether the same is applicable in humans also and conducted a study among 45 participants, in which they found...

### **...CORRELATION BETWEEN HIGHER ALCOHOL WITHDRAWAL SEVERITY AND GREATER DISRUPTION IN THE CORTICOSTRIATAL REGION...**

...through functional magnetic resonance imaging (fMRI), coupled with an increase in heavy drinking. Following this, they further went ahead and conducted a placebo-controlled randomized controlled trial (RCT) with 23 participants of alcohol dependence and demonstrated that (2)...

### **...PRAzosin TREATMENT AT A DOSAGE OF 16 MILLIGRAM PER DAY EFFECTIVELY AMELIORATED THIS DYSFUNCTION, LEADING TO SUBSTANTIAL ENHANCEMENTS IN ALCOHOL TREATMENT OUTCOMES WITHOUT MAJOR ADVERSE SIDE EFFECTS.**

The combined findings underscore the pivotal role of alcohol withdrawal in precipitating alcohol-related prefrontal striatal dysfunction, offering a promising avenue for intervention through prazosin or its congener doxazosin with favorable pharmacokinetic profile of once-a-day dosing.

### **APREMILAST:**

Immune and inflammatory pathways, more specifically cyclic adenosine monophosphate specific (cAMP-specific) phosphodiesterase type 4 (PDE4) has been proposed to be critical regulator of AUDs. PDE4 inhibitor apremilast, a drug used in management of psoriasis with an excellent safety profile, has been tried in the recent years for treatment in AUDs.



A study involving multiple animal strains and models as well as in humans was conducted recently. A significant reduction in binge drinking, motivation to drink, alcohol dependence, and increased neuronal activity in nucleus accumbens was seen in animal models. In the phase IIa double-blind, placebo-controlled, Proof-of-Concept (PoC) study involving 43 participants that achieved an impressive 84% completion rate,...

### **...APREMILAST DEMONSTRATED A SIGNIFICANT REDUCTION IN DAILY ALCOHOL CONSUMPTION AND A LOWERED LIKELIHOOD OF HEAVY DRINKING IN COMPARISON TO A PLACEBO.**

Furthermore, apremilast exhibited potential in reducing alcohol craving, albeit accompanied by mild side effects (3). Apremilast holds promise as a therapeutic option for AUD both for reducing heavy drinking and reducing craving of alcohol.

### **STUDIES RELATED TO NEUROIMAGING AND NEUROMODULATION**

Studies related to effects of chronic alcohol intake on the brain has found dysregulation of the dopaminergic system, i.e., hypofunction of dopaminergic activity and decreased release in the nucleus accumbens, reduced number of D2 receptors in the ventral striatum, and decreased dopamine release in the limbic striatum. On the other hand, artificially increasing the number of D2 receptors in a preclinical study was associated with reduction of alcohol intake. These initial findings encouraged researchers to stimulate the dopaminergic system with high frequency repetitive transcranial magnetic stimulation (rTMS) to the right dorsolateral Pre-Frontal Cortex (dlPFC) (4). Stimulation to superficial structures like dlPFC and insular cortex yielded mixed results in the past, which generated the idea to stimulate deeper specific regions in the brain. A double-blind, randomized, sham-controlled proof-of-concept trial encompassing 51 recently abstinent treatment-seeking patients, with

### **...DEEP REPETITIVE TRANSCRANIAL MAGNETIC STIMULATION (dTMS) OF FIVE SESSIONS PER WEEK FOR THREE CONSECUTIVE WEEKS TARGETING DEEPER STRUCTURES...**

...like midline frontocortical areas including the medial prefrontal and anterior cingulate cortices...

### **...YIELDED MARKED CLINICAL AND NEUROIMAGING IMPROVEMENTS.**

Unlike many previous studies, in this study, dTMS was always preceded by craving induction, where the participant would hold and smell the beverage of his choice but not consume it. The effects were seen up to 12 weeks after completion of the acute phase of treatment (5). This study indicates that in selected patients with AUD, rTMS may be tried as a treatment option. The newer drugs and neuromodulation techniques hold promise for improving the outcomes in patients with AUD.



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# RECENT ADVANCES: ILLICIT SUBSTANCES

VINIT PATEL(1), MOHITA JOSHI(2), AMIT SINGH(2)

(1) AIIMS, NEW DELHI; (2) KGMU, LUCKNOW

## MANAGING SLEEP DISTURBANCES IN PATIENTS ON OAT

Sleep is a common problem at various phases of Opioid use disorder (OUD), including in patients maintained on Opioid Agonist Treatment (1). Managing sleep disturbances in this population is difficult as conventional medications such as benzodiazepines can be abused and are associated with increased mortality in this population. Evidence for using other sleep medications is scarce. Against this backdrop, a double-blind, placebo-controlled RCT from India is important. In this study, 100 men with opioid dependence maintained on buprenorphine reporting sleep disturbances were provided trazodone or placebo for their sleep problems and reassessed after six weeks.



SLEEP

**THE STUDY REPORTED SIGNIFICANT IMPROVEMENT IN SLEEP QUALITY, LATENCY, EFFICIENCY, AND DURATION WITH A MEAN TRAZODONE DOSE OF AROUND 100 MILLIGRAMS DAILY.**

Other factors, such as improvement in depression, anxiety, or opioid withdrawal symptoms, could not account for the improvement in sleep. It also found trazodone to be well tolerated with minimal drop-outs (2). The long-term efficacy as well as patient acceptability of the medicine needs further study.

## SEXUAL PROBLEMS AND OPIOID USE DISORDER

Another concern with OUD is sexual problems in patients with OUD. In this regard,...

**...A SCOPING REVIEW BY INDIAN RESEARCHERS REPORTED HIGH PREVALENCE OF SEXUAL DYSFUNCTION IN ALCOHOL AND OPIOID USE DISORDERS. ERECTILE DYSFUNCTION (ED) WAS THE MOST STUDIED AND REPORTED SEXUAL DYSFUNCTION.**

The prevalence of ED also varied based on treatment group, different studies reported different prevalence with a comparative excess in methadone or naltrexone group as compared to buprenorphine group. Prevalence of ED reduced after starting methadone (3).



Another comparative study from India assessing sexual behavior, dysfunction, satisfaction, relationship, and quality of life between treatment naïve and buprenorphine maintained OUD patients. Frequency of ED and premature ejaculation (PME) were significantly more in treatment naïve group than in the buprenorphine group. Buprenorphine group had better satisfaction, sexual relationship, and quality of life (4).

## PRENATAL EXPOSURE TO ILLICIT DRUGS AND FETAL OUTCOMES

A birth cohort study from Taiwan examined association of prenatal illicit drug exposure and risk of developing neurodevelopmental disorders (NDD) and disruptive behavioral disorder (DBD). The investigators used data from four national databases, traced children from birth to 7 years, and identified those diagnosed with NDD. Hazard ratio with prenatal exposure to illicit drugs for developmental delay, intellectual disability, attention deficit hyperactivity disorder and DBD were 1.54 (95 % CI: 1.21–1.95), 2.63 (1.64–4.19), 1.58 (1.23–2.03) and 2.57 (1.21–5.48), respectively (5).

## PRENATAL METHAMPHETAMINE EXPOSURE WAS ASSOCIATED WITH DEVELOPMENT OF NDD AND DBD IN OFFSPRING, WHILE PRENATAL OPIOID EXPOSURE WAS ONLY ASSOCIATED WITH NDD IN THE OFFSPRING.

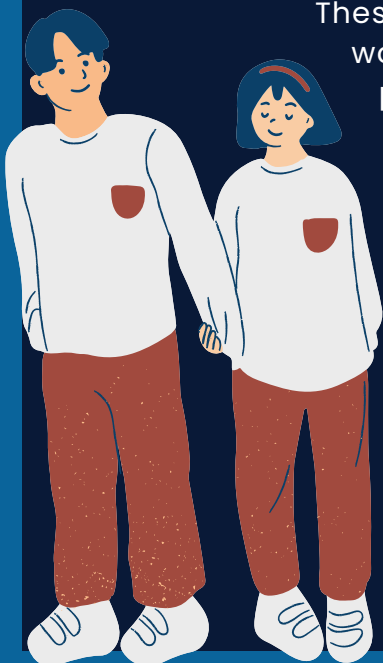
A retrospective chart review by researchers from the USA evaluated the effect of cumulative duration of prescription opioid use exposure during pregnancy, timing (late as third trimester), and outcome measure being the neonatal opioid withdrawal syndrome (NOWS) in the first 30 days after delivery. The researchers reported...

## ...OPIOID EXPOSURE FOR MORE THAN 30 DAYS DURING PRENATAL PERIOD WAS ASSOCIATED WITH NOWS, WHILE THIRD-TRIMESTER OPIOID EXPOSURE, IRRESPECTIVE OF DURATION OF EXPOSURE, ASSOCIATED WITH NOWS(6).

These studies underscore the need to regularly screen pregnant women for illicit substances and offer appropriate treatment to prevent adverse fetal and neonatal outcomes.

## IMPACT OF RECREATIONAL CANNABIS USE: FINDINGS FROM A TWIN STUDY

Various geographies are modifying their cannabis laws to allow medical or recreational cannabis use; however, the effect of such legislation is not well understood. A group of researchers from USA tried to assess this through a longitudinal, co-twin control design study in 4043 twins (7). They identified 240 twin pairs which were discordant for residences in terms of legalization of recreational cannabis use (one twin was living in a state where recreational cannabis use was legalized, while



the other was living in a state that had not legalized recreational cannabis use). The pairs were first assessed at adolescence and then currently at age 24–49 years. They found that the...

### **...TWIN LIVING IN A RECREATIONAL STATE USED CANNABIS MORE OFTEN AND HAD FEWER ALCOHOL USE AS COMPARED TO TWIN LIVING IN NON-RECREATIONAL STATE.**

Cannabis legalization caused a 0.11 standard deviation (SD) increase in cannabis frequency, whereas AUD symptoms decreased by 0.11 SD driven by reductions in use of alcohol when physically hazardous. There was no increase in cannabis use disorder at individual level, nor any change in alcohol or illicit substance consumption. There was no relationship between recreational cannabis use and psychoticism. Clearly, the debate on the impact of recreational cannabis use remains alive.

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# RECENT ADVANCES: SPECIAL POPULATIONS

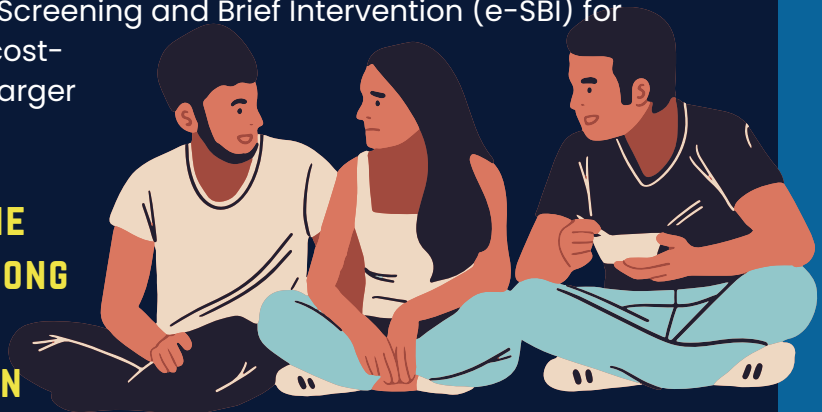
GAYATRI BHATIA

AIIMS, RAJKOT

## DIGITAL INTERVENTIONS FOR SUBSTANCE USE DISORDERS IN ADOLESCENTS

The term 'digital health interventions' denotes services delivered with the support of technology including targeted client communication; personal health tracking; and on-demand information access (1). Electronic Screening and Brief Intervention (e-SBI) for substance use offers flexibility, anonymity, cost-effectiveness, and the potential to reach a larger proportion of the population in need.

**TWO RECENT META-ANALYSES ON THE EFFICACY OF STANDALONE E-SBI AMONG SUBSTANCE-USING ADOLESCENTS INDICATED SIGNIFICANT REDUCTION IN ALCOHOL, TOBACCO AND CANNABIS USE AMONG ADOLESCENTS (1, 2).**



However, the feasibility and applicability of e-SBI in Indian substance using youth were hitherto unexplored. A recently conducted mixed methods randomized controlled trial conducted on 219 college students from North India, with a follow-up duration of 3 months, has reported that e-SBI is feasible, acceptable and effective in reduction of alcohol and cannabis use among Indian youth, with multiple sessions of brief intervention being associated with a greater effect size (3). These findings open new avenues for large scale preventive initiatives for substance use among adolescents, and may be included in government programmes for substance use prevention.

## SMARTPHONE ADDICTION AMONG ELDERLY

Problematic internet and smartphone use are issues generally associated with adolescents and youth. However, recent studies indicate that an increasing number of older adults have adapted to using smartphones and spend a significant part of their day using them (4). Empirical evidence from China, in the form of two cross-sectional surveys on 371 and 656 elderly participants indicated that (4, 5)...

**...SUBJECTIVE COGNITIVE DECLINE, FAMILY CONFLICT, LONELINESS AND ALIENATION WERE SIGNIFICANTLY ASSOCIATED WITH SMARTPHONE ADDICTION.**



Similar reports from Brazil, Korea, and Japan express concern over smartphone dependence in the elderly. Cross-sectional studies from China and Japan, involving more than 600 elderly participants, also report a (6)...

### **...SIGNIFICANT ASSOCIATION OF SMARTPHONE ADDICTION AMONG THE ELDERLY WITH POOR SLEEP QUALITY AND HIGHER SCORES ON DEPRESSION AND ANXIETY SCALES.**

As India witnesses increasing urbanization and breakdown of the joint family system, rising cases of smartphone addiction may be anticipated in the elderly. Systematic research directed towards understanding smartphone dependence among elderly and exploration of preventive and management initiatives are recommended.

### **DRUG POLICIES AND WOMEN WITH SUD**

Substance use in women is associated with unique physical and psychosocial vulnerabilities posing particularly complex challenges in pregnancy, including neonatal abstinence syndrome, low birth weight, and premature birth. Women with SUD are at a higher risk of violence, trauma, discrimination and involvement with sex work, issues which require gender-specific policy responses and intervention framework. However, (7)...

### **...A RECENT REVIEW OF DRUG POLICIES OF NINE COUNTRIES, INCLUDING INDIA (BOTSWANA, CROATIA, EGYPT, INDIA, THE NETHERLANDS, NORTH MACEDONIA, POLAND, PORTUGAL, AND PAIN) REVEALED LIMITED ADHERENCE TO THE UNODC CHECKLIST FOR GENDER MAINSTREAMING IN PROJECTS/PROGRAMS.**

All countries reviewed had epidemiological data on substance use among women and had performed a background situation analysis. Gender sensitivity was evident in themes of treatment and prevention, followed by training of healthcare providers, but issues related to violence, punitive legislations for pregnant women and laws regarding children's custody for mothers were neglected or inadequately covered. These findings may encourage advocacy, research and upgradation of drug related policies in order to holistically incorporate provisions for the unique psycho-social needs of women with substance use disorders.







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# RECENT ADVANCES : NEWER ISSUES

VENKATA LAKSHMI NARASIMHA, SHALINI KUMARI  
AIIMS, DEOGHAR

## NITAZENE: AN OLD DRUG, NEW FACE

### **NITAZENES, OR “FRANKENSTEIN OPIOIDS,” ARE $\mu$ -OPIOID RECEPTOR AGONISTS WITH A DISTINCT HISTORY.**

After its discovery in the 1950s, it was largely forgotten for several decades until its re-emergence in the illicit drug market in Belgium and Canada as a street drug in 2019. The sudden appearance of nitazene as a street drug in 2019 caught the attention of law enforcement agencies, sparking concern about its potential consequences. Nitazene contributed to 5% of overdose related deaths in 2021. Similar...

### **...OTHER NOVEL POTENT OPIOIDS (NPOs) SUCH AS ISOTONITAZENE AND BRORPHINE HAVE BEEN FOUND IN STREET HEROIN SAMPLES.**

These NPOs are 1000 times more potent than morphine and account for overdose (OD). [Amaducci et al.](#) (2023) reported that...

### **...NALOXONE REQUIREMENT FOR THOSE WITH OD WITH NPOs IS MUCH HIGHER COMPARED TO OD WITH FENTANYL.**

They conducted a subgroup analysis of a national, multicentre study to investigate non-fatal opioid OD, in their latest study in JAMA network open (1). Along with fentanyl, NPOs are emerging as a significant public health concern with greater health damage.

## SUBSTANCE-INDUCED PSYCHOSIS TO INDEPENDENT SCHIZOPHRENIA

The debate of the link between cannabis and schizophrenia is a long standing one. Other substances, including amphetamine type stimulants, are known to cause acute psychotic episodes. How many of these progress on to develop schizophrenia was studied by [Myran et al.](#) (2023) through a population-based retrospective cohort study. It was found that...

### **...INDIVIDUALS WITH SUBSTANCE-INDUCED PSYCHOSIS HAD A 163-FOLD HIGHER RISK OF TRANSITIONING COMPARED TO THE GENERAL POPULATION.**



Among those with psychosis, cannabis use had the highest transition risk. Younger age and male gender were also linked with a greater transition risk (3). This study becomes important in the context of changing cannabis legislation across the world.

## DEEP BRAIN STIMULATION (DBS), FAECAL MICROBIOTA AND ADDICTION

As we read about the recent popularity of DBS for mental illness and how it is regulated by the Mental Health Care Act 2017, we wonder about its efficacy and role in Addictive Disorders. A recent systematic review suggested that (4)...

### ...DBS TARGETING NUCLEUS ACCUMBENS (NAC) REDUCED RELAPSE RATES TO 8%.

NAC is a commonly targeted site for OCD and Depression. Interestingly(5)...

### ...A RECENT PHASE-1 RANDOMIZED CONTROL TRIAL SHOWED THE POTENTIAL OF FAECAL MICROBIOTA TRANSPLANTATION IN REDUCING ALCOHOL CRAVING.

Exploring these newer modalities to assist people in quitting substances is an intriguing prospect.

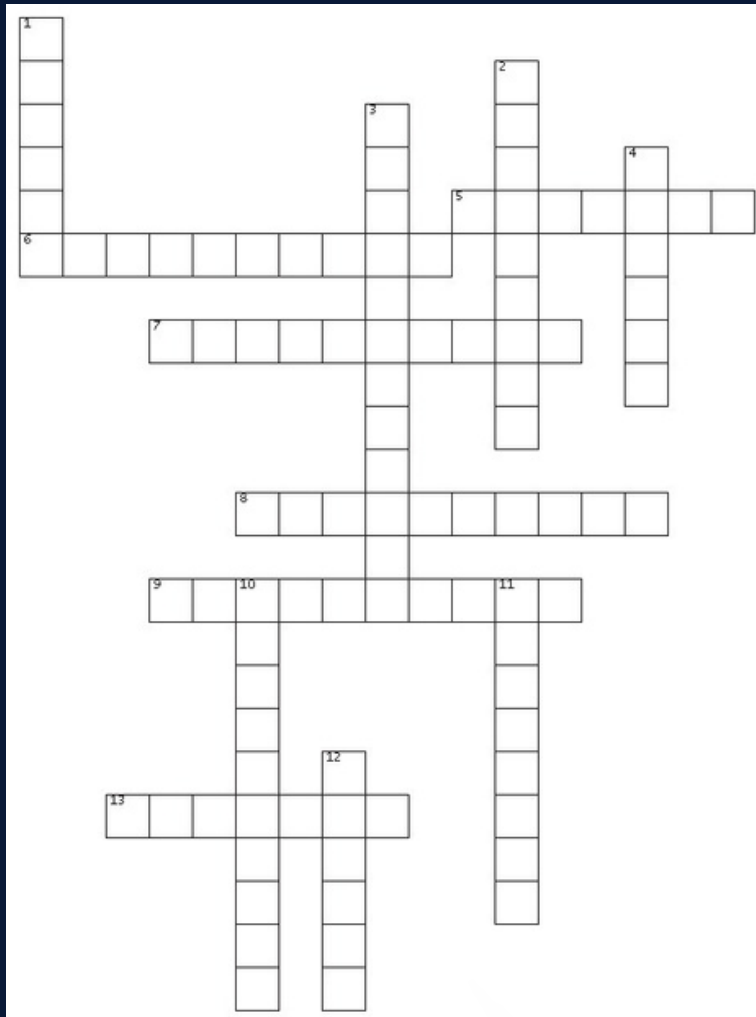
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# APSI MINDBENDER CHALLENGE YOUR BRAIN!!

PREETHY KATHIRESAN  
AIIMS, NEW DELHI



## ACROSS

- 5.- First country to legalise cannabis use or recreational purpose in December 2013
- 6.- Earlier used as an aversive agent, currently being used as a deterrent agent in treatment of alcohol dependence
- 7.- Gradual change in the homeostatic set-point for hedonic state caused by repeated intake of drugs
- 8.-The antidote for methanol poisoning
- 9.- An anticraving agent which also has been found to help in reducing impulsivity
- 13.- The country which temporarily withdrew from the UN 1961 Single Convention as a protest against the classification of coca leaves as a narcotic drug

## DOWN

- 1.- Treating patients with drug dependence is a type of \_\_\_\_\_ reduction strategy of drug control
- 2.- An antidepressant used in management of nicotine dependence
- 3.-The active metabolite formed when Alcohol and cocaine are taken simultaneously
- 4.- Prohibition of use of a substance in an area is considered as a type of \_\_\_\_\_ reduction strategy of drug control
- 10.- The 1st non-opioid medication which got FDA approval for management of opioid withdrawals
- 11.- Drug of choice to manage Opioid Overdose
- 12.- Gamma hydroxy butyrate is also called as \_\_\_\_\_ Ecstasy

# ADDICTION: A SWEET POISON

LOVE TOMAR

AIIMS, NEW DELHI

The tale of addiction runs through time untold,  
A swirling vortex, demanding tolls untold,  
Where does it lead, for those it ensnares?  
Dark shadows cast; humanity ensnares.

As infants we begin on a pristine page,  
As we age, our thoughts and friends change,  
A thirst for new experiences, it rises,  
Everyone lauds youth's innocent guises,  
On TV, at home, with peers, all do,  
"Let's smoke and drink," their voices pursue.  
But the moment it starts, it's hard to cease,  
Its dark shadows upon humanity increase.



With friends, we drank, raced, and cheered,  
Our spirits peaked, but now fear leered,  
The beer we shared on Saturdays, was such a delight,  
Our worries lifted with each gulp, taking flight,  
We stumbled home after, late at night,  
Addiction's shadows grew strong in our sight.

As years went by, habits altered with time,  
Saturday's revelries soon became every night's climb,  
From beer to rum, then whiskey, we strode,  
A whole bottle consumed, nothing better to behold,  
Sometimes bhang, ganja, or charas too,  
Smoke rings filled the air, laughter ensued.  
But two puffs, and we felt so light,





We couldn't reach home some nights,  
Addiction's hold grew, so deep and tight,  
Its shadows loomed, blocking out the light.

Friends parted, work began, life anew,  
Drinking alone at home, each night anew,  
Sweat poured, and the situation worsened,  
Now drinking began from morning, addiction strengthened,  
Tea replaced by a glass of wine,  
Counting stars and not sleeping, he'd whine.

Addiction's shadow cast all over his life,  
A tavern he saw instead of a world rife,  
With a barkeeper as company, alien to all,  
Addiction grew stronger, as he began to fall.



No consciousness, no regret, no improvement,  
Only drinking, its shadow cast with each movement,  
Voices echoed, ghosts appeared, hands shook,  
Money, friends, job lost, relationships broke,  
His wife left him, cut all ties, addiction hugged,  
Its shadow upon humanity, forever tugged.

His body deteriorated, complaints of jaundice and weakness,  
but he kept on drinking, the only thing he could access,  
Doctors tried, but he couldn't be saved,  
One day he seized, in the ICU he lay, braved,  
Mental illness cured, only then could his body heal,  
Addiction recovery, a psychiatrist revealed.

In rehab, he questioned why he was there,  
"Why am I sick, when everyone else is fair?"  
Death was acceptable, a world that jeered,  
Addiction's shadow, humanity feared.

But therapy changed him, and group sessions too,  
Others shared their tales, tears were no taboo,  
His spirit grew, food and sleep he enjoyed,  
Cravings decreased; the future no longer destroyed.

His extinguished light, now shone bright,  
Happiness and confidence, back in sight,  
Addiction's shadow, still loomed large,  
But he vowed freedom, as he left that barge.

How many homes have been destroyed?  
Desires ruined, dreams unemployed?  
Parents weeping, children left alone,  
Why do we ignore it, addiction's tone?  
Mental illness it is, we must understand,  
Together we can fight, its shadows unmanned.



# मेरी कहानी

VEERENDRA VIKRAM  
ARMED FORCE MEDICAL SERVICES

पीढ़ियों से परिवार में इसका खाता है; बचपन से ही शराब से मेरा नाता है।  
देखा है मैंने आते डगमगाते; कभी डांटते, तो कभी डांट खाते।  
होती थी हर रोज़ लड़ाई; कभी वाक्युध तो कभी हाथापाई।  
सोचते थे, आखिर ये चलेगा कब तक; डरे सहमे रहते थे हम दर्शक।  
शराब है बुरी चीज बात तब ये समझ आई; पीऊंगा ना कभी कसम थी मैंने खाई।  
घर के माहौल ने असर था मुझपर डाला; मैं हुआ डरपोक, कमजोर और बेचारा।  
लोगों को मिलने से मैं कतराता; पर दोस्त की दोस्ती खूब निभाता।  
स्कूल में साथी दबू कहकर चिढ़ाते; क्लास का मुर्गा और बकरा अक्सर मुझे बनाते।  
साथी है, सोच कर रह जाता; दर्द तो होता था पर नहीं कह पाता।  
यूँ ही करते सहते हो गया दसवी पास; सोचा इंटर कालेज में करेंगे नई शुरुआत।  
नए कालेज में कुछ तो बदले हालात; मुझे मिल गया कुछ दोस्तों का साथ।  
पर इनका पढाई पर नहीं था जोर; गर्लफ्रेंड किसकी पहले, ये थी होड़।  
शौक थे तफरी, पार्टी और सिनेमा; क्लास में हाजिरी हो पूरी था मेरा जिम्मा।  
दिल के तो थे मेरे भी अरमान; पर काम नहीं था ये आसान।

हालत पर मेरी, दोस्तों को तरस आया; हिम्मत बढ़ाने का अचूक उपाय सुझाया।  
महफिल में सब बैठे थे एक शाम; मुझे भी थमा दिया शराब का एक जाम।  
फिर मेरी हुई खूब हंसाई; जब मैंने न पीने की कसम बताई।  
सोच ले तू क्या चाहेगा; हमारे साथ पीना है या छोड़कर जायेगा।  
मुझे थी दोस्तों की दरकार; बस एक बार पीने को हो गया तैयार।  
नाक बंद करके पी गया एक जाम; नहीं याद उसके बाद कैसे बीती शाम।  
अगले दिन फिर कसम थी खाई; पर वो भी ज्यादा दिन न चल पाई।  
और कुछ ही दिनों के बाद; हम सब फिर बैठे साथ-साथ।  
दोस्त के जन्मदिन का था मौका; बोला, तू कैसे रहेगा सूखा।  
ना ना करते पी गया प्याला; अबकी तो था असर निराला।  
सच कहूँ तो मजा आ गया; बकरा जैसे शेर खा गया।  
फिर अवसरों पर लगा में पीने; ऐसे निकले कई महीने।  
स्कूल, कालेज सब हो गया पास; नौकरी की हुई तलाश।  
जैसे ही मैंने नौकरी पाई; घरवालों ने की सगाई।



आज भी याद है अपनी शादी; दोस्तों ने जब मुझे पिला दी ।  
फिर तो पीना हो गया आम; हर छुट्टी छलकाए जाम ।  
धीरे-धीरे चाह बढ़ गई; छुट्टी छोड़ हर शाम पर अड़ गई ।  
जीवन में कुछ मुश्किल पड़ गई; मेरी शराब यूँ ही बढ़ गई ।  
पैग तो क्या क्वार्टर से भी न होता आराम; दिन भर सोचूँ कब होगी शाम ।  
काम अधूरा छोड़ कर भागूँ; पियूँ नहीं तो देर रात तक जागूँ ।  
हुआ शुरू हाथों का कंपन; बदल गया फिर मेरा जीवन ।  
शराब के बिन लगे मुश्किल जीना; सुबह उठते ही शुरू हो जाऊँ पीना ।  
पत्नी ने, बॉस ने, सब ने डांटा; मेरा दर्द पर शराब में बांटा ।  
बोले सब छोड़ दो, पड़ेगी भारी; पर कोई न समझा मेरी लाचारी ।  
अब किस-किस को समझाऊ; छोड़ना चाहूँ पर रोक न पाऊँ ।  
तस्वीर, नाम, सुगंध और तीखी बात; बढ़ाएँ ललक, मुश्किल करें हालात ।  
भोजन छूटा, आई कमजोरी; बनाई शराब से दूरी थोड़ी ।  
एक ही दिन था रोक में पाया; फिर अचानक सर चकराया ।  
होश आया तो अस्पताल में पाया; मुझको था दौरा आया ।  
डॉक्टर बोले चाहते हो जीना; बंद कर दो बिलकुल पीना ।

फिर महीने भर न हाथ लगाया; घरवालों ने भी साथ निभाया ।  
छूट गई अब, हो गया भरोसा; पर जल्दी ही खा गया धोखा ।  
एक पुराना दोस्त टकराया; खाने पर उसने मुझे बुलाया ।  
देख के बोतल लालच आया; पर नहीं पीऊंगा उसको समझाया ।  
तू मत पीना हम पी लेंगे; बैठ तो सही बचपन जी लेंगे ।  
हाथ में जूस, नज़र जाम पर; खुद को रोक पाना हो गया दूभर ।  
महफ़िल, शराब, और शाम; जग गए सोये अरमान ।  
मैं थोड़ा सकुचाया, तुरंत दोस्त ने जाम थमाया ।  
एक ही पीऊंगा सोचा मैंने; पर पी गया जाने कितने ।  
अब पी ली तो कुछ दिन और है पीना; कसम से छूऊंगा फिर कभी ना ।  
ऐसे उतार-चढ़ाव जाने कितने आए; थोड़ी थमे फिर आगे बढ़ जाए ।  
फिर एक दिन मिले एक सुभचिन्तक; बोले तुम्हें चाहिए मनोचिकित्सक ।  
पागल नहीं मैं, विरोध जताया; बोलो किसको मारा, कब नाली में पाया ।  
पीते हैं जाने कितने मुझसे ज्यादा; फिर मुझ पर ही क्यों निशाना साधा ।  
सच कहूँ तो बीमारी की थी मुझे भी शंका; पर मैं हूँ शराबी बजे क्यों डंका ।  
काफी ना-नुकर के बाद हो गया राजी; अस्पताल पहुंच गया अब इलाज है बाकी ।

# ART WORK

DHEERAJ KATTULA

CMC, VELLORE





# Reader's Feedback

PERSONAL EXPERIENCE/ NARRATIVE/ PAINTING/ POEM

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