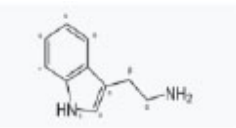

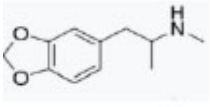


(Table 3) contd....

Substance	Antidote	Exposure	Treatment	Symptoms	Neurotransmitter/pathways/receptors Implicated	Chemical Structure
Hallucinogens (Tryptamines)	Naloxone	Inhalation, Intravenous, Oral	The main chemical is in a kind of mushroom, so do not misuse	Perception will be interrupted, and alteration in the perception, spontaneous reoccurrence of perceptual disturbance, and the illusion of movement will exist.	All three subgroups share a common mechanism in the serotonergic system, represented by the agonism/partial agonism at the 5-HT _{2A} receptor (activation), 5-HT _{1A} , and 5-HT _{2C} . However, Various hallucinogenic/psychedelic substances might have distinct interactions with various neurotransmitters, such as NMDA receptors, σ -receptors, μ -opioid receptors, and muscarinic receptors, in addition to their ability to inhibit serotonin and dopamine reuptake at their respective transporters.	 C ₁₀ H ₁₂ N ₂
Phencyclidine	Diazepam, haloperidol, chlorpromazine	Smoking, by mouth, snort, injection.	Medical care	PCP exhibits more intense psychotic effects, such as hallucination and delusion, especially illogical thinking (79). Apathy (lack of interest), decreased talking, repetitive speech, and catatonic posturing (unusual body movements).	-	 C ₁₇ H ₂₅ N
Entactogens, (MDMA)	Medical care	delusions (96%), hallucinations (96%), disorganization (96%). Feeling down (90%) with reduced emotional expression (81%), (77).	-	-	-	 C ₁₁ H ₁₅ NO ₂
Antibiotics	Use them in a limited amount.	-	-	-	-	-

Note: MDMA: 3,4-Methyl enedioxy methamphetamine, commonly known as ecstasy.

3.6. Amphetamine

Amphetamine is a strong central nervous system stimulant. Amphetamines, such as methamphetamine and 3,4-methylenedioxyamphetamine (MDMA), belong to a class of compounds called phenethylamines that induce catecholaminergic effects in the CNS and peripheral circulation. Nowadays, amphetamines are clinically used to treat short-term obesity, narcolepsy, and attention deficit disorder with hyperactivity [22]. Due to recent studies, psychosis following amphetamine use is characterized by delusions, visual hallucinations, and symptoms resembling acute psychosis most commonly observed in schizophrenia. There is an obvious pattern of high dosage and daily usage correlating with higher risks of substance-induced psychosis. Amphetamines impair the cognitive thought process and precede acute psychosis. This shows that continued impairment due to amphetamine use is a precursor to psychosis. (Table 3) [23, 24].

3.7. Cocaine

Cocaine is one of the most common substances that leads to transitory paranoia [25]. Cocaine is widely recognized to be associated with several mental disorders, and its use develops psychotic symptoms. Cocaine works as an inhibitor of serotonin and noradrenaline reuptake. The majority of psychotic symptoms are related to cocaine use within 24-48 hours [26, 27]. In sum, it is one of the most favorite drugs among teenagers and can be a serious risk factor and increase the possibility of psychoses in the future [28, 29] (Table 3).

3.8. Kratom

Kratom (*Mitragyna speciosa*) is a psychoactive plant preparation that has medicinally been used for its stimulant effects and as an opioid substitute [30]. It can cause psychosis and even death. But the difference is that kratom's effect for causing psychosis is stronger than

other opioids. It can lead to addiction, sleeping and eating disorders as well. Also, neuropsychiatric side effects such as hallucinations, delusions and paranoia are usual after kratom intake [31] (Table 3).

3.9. Cathinone

Cathinone is related to the phenethylamine family but its potency is much lower than others [32]. It starts to have effects on consumers within 15 minutes at least and 45 minutes at most after injection. By inhaling, the sensations can be experienced within minutes and reach a higher intensity and stronger effect, but the effects last for 2-3 hours in oral and nasal use [33, 34]. This group consists of substances similar to the ones naturally occurring in *Catha edulis* (Khat) known as cathinone [35] (Table 3).

3.10. Hallucinogens

Hallucinogens include a wide group of natural and synthetic substances. As hallucinations are the intended toxidrome, these substances may cause psychosis. Currently, classic hallucinogens are seen as those that have a psychopharmacological profile similar to mescaline, psilocybin, and lysergic acid diethylamide (LSD) [36]. Classical hallucinogens (psychedelics) can be divided into three main chemical classes: tryptamines (*e.g.*, psilocin), ergolines (*e.g.*, LSD), and phenethylamines (*e.g.*, mescaline). Tryptamines closely resemble serotonin chemically. Psilocybin and mescaline are natural, but LSD and LSD-like are synthetic drugs. It affects the visual cortex, which leads to illusions and open-eye dreams, which is one of the most important psychotic symptoms *ref.* There are two kinds of perception disorders by using hallucinogens: *short-term*, in which users do not experience significant impairment; psychiatric care is rarely sought; and *long-term*, which reflects chronic severe syndrome [37, 38] (Table 3).

3.11. Phencyclidine and Ketamine

These effects can be attributed to dopamine level increment in the prefrontal cortex, which can be understood by considering the binding of ketamine and PCP to the dopamine receptor 2 (D2) [[39, 40]. Beck and coworkers discovered a noteworthy increase in temporary

mental health issues related to ketamine usage [38, 41-43] (Table 3).

3.12. Antibiotics

Surprisingly, some kinds of antibiotics can lead to psychotic disorders (*e.g.*, fluoroquinolones) [44-47] (Table 3).

3.13. Miscellaneous Compounds

Although, these are not the only substances that may lead to psychosis. There are other substances that can lead to psychosis; Dissociative, Sedatives or analgesics, New synthetic opioids (NSOs) (*e.g.*, U-47700, U-49900, AH-7921, U-50488, U-51754, MT-45, Acetylfentanyl, Carfentanyl, Furanylfentanyl) [48], Desomorphine ('krokodil'), Mitragynine ('Kratom', 'kakuum', 'thang', 'ketum', 'biak') [49], Salvinorin A (*Salvia divinorum*, *hierba de Maria*, 'Maria pastora', 'Sally-D', 'magic mint') [50], Ketamine-like dissociatives; Ketamine ('ket', 'special K', 'super K', 'kit-kat') [51], Phencyclidine (PCP, 'angel dust', 'supergrass', 'boat') and PCP-type substances (*e.g.*, 3-MeO-PCE, 4-MeO-PCP) [52], Methoxetamine ('mexxy', 'special M'), Novel Stimulants and novel psychedelics [53]; Synthetic cathinones (*e.g.*, mephedrone, 'm-cat', 'meow') [54], Psychedelic/empathogenic phenethylamines (*e.g.*, 2C series; D series, such as DOI, DOC; benzodifurans, such as 'bromodragonfly'; others, such as PMA/PMMA) [55], Piperazines (*e.g.*, BZP, mCPP, 'party pills', 'smileys') [56], Tryptamines (*e.g.*, DMT, 5-MeO-DMT, 'magic mushrooms'), Prescription drugs with a misusing potential: 1. ANTIDEPRESSANTS; (Bupropion, Amitriptyline, Venlafaxine ('baby ecstasy')) [57], 2. ANTIPSYCHOTICS: (Quetiapine ('Susie Q', 'Quell', and 'baby heroin'); 'Q ball' (quetiapine with cocaine); 'MaQ ball' (quetiapine and marijuana), Olanzapine ('Lilly')) [58], 3. GABAPENTINOIDS (pregabalin and gabapentin), 4. Z-DRUGS (zaleplon, zolpidem and zopiclone) [59], DESIGNER BENZODIAZEPINES (*e.g.*, clonazolam, etizolam, flubromazepam, phenazepam ('Zinnie') and pyrazolam [60], 5. OVER-THE-COUNTER DRUGS: (Codeine [61] ('Purple drank' is a mix of codeine and promethazine), Loperamide [62], Dextromethorphan (DXM) [63] for instance [64-72] (Tables 3 and 4).

Table 4. Psychoactive substances or medications causing secondary psychosis.

Medical Section	Category (type)
Psychoactive Substances	Alcohol Withdrawal and Hallucinosis, Amphetamine Intoxication, Cocaine Intoxication, Hallucinogen Intoxication, Phencyclidine Intoxication, Sedative Hypnotic Withdrawal
Cardiology	Digitalis, Beta-blockers, Antiarrhythmics
Oncology	Asparaginase, Cytarabine, Fluorouracil, Ifosfamide, Methotrexate, Vincristine
Infectious diseases	Ciprofloxacin, Antitubercular agents, Antimalarials, Antivirals
Neurology	Dopamine agonists (amantadine, bromocriptine, and levodopa)
Psychiatry	Antidepressants (bupropion, tricyclic antidepressants), Anticholinergics (benztropine, diphenhydramine)
Gastroenterology	Cimetidine, Ranitidine
Analgesia	Pentazocine, Meperidine, Indomethacin
Genera	Corticosteroids, Metrizamide, Methysergide, Baclofen Ephedrine

4. DISCUSSION

In the last two decades, plenty of research has been dedicated to psychosis induced by cannabinoids, psychostimulants such as methamphetamine, amphetamine, methylphenidate and cocaine, hallucinogens and so on. Despite the apparent connection to psychotic symptoms, the scientific community is still unable to give definitive proof on this specific subject. The main point about the subject is that there has been a notable rise in both the quantity and diversity of newly developed psychoactive drugs. Over time, more powerful have been formulated and circulated, resulting in more harmful side effects and more severe impacts on the body. This surge in new drug misuse has greatly expanded the occurrence of secondary psychoses.

For example, synthetic cannabinoids and synthetic cathinone may lead to serious clinical syndrome with a high risk of a fully structured psychotic disorder [73, 74]. Clinicians still face a difficult task in differentiating SIP and primary psychotic illnesses. Nonetheless, we hold optimistic expectations that this research could assist in overcoming the challenge [75, 76].

But despite considerable variation in how substance exposure and psychosis were elicited or defined, there is a notable consistency across the population groups studied in different research. As has been said before, young ages play a big role in drug abuse. The most common reasons are fun or parents' attitudes. On the other hand, drug abuse may have real side effects on the body and especially the brain as time passes and may lead to psychosis in the future. Although none of these variables, alone or together, can recognize the etiology of psychosis accurately. A combination of approaches is the best management for substance-induced psychosis, which includes medication management, psychological treatment (individual therapy or group therapy), and family engagement in some cases. After all, we have collected as much information as we could about different drugs that may lead to psychosis, psychotic symptoms, and similarities and differences between such substances. Finally, this article has been based on limited evidence, and further study of both pharmacologic and psychological interventions is needed to find out how to provide the best care to vulnerable youth and adults who have experienced such symptoms of psychosis and substance use. Systematic literature reviews are crucial in research articles for several reasons. For example, they provide a comprehensive overview of existing research on a particular topic, helping researchers understand the current state of knowledge. By following a systematic approach, researchers can ensure that the review is unbiased and based on all available evidence, reducing the risk of cherry-picking data. Systematic reviews help identify gaps in the existing literature, highlighting areas where further research is needed. They allow for the evaluation of the quality of individual studies, helping to assess the reliability of the findings. Also, systematic reviews can facilitate meta-analysis, where data from multiple studies are combined to provide more robust conclusions. The results of systematic reviews can inform policy-making, clinical practice, and future research

directions. Overall, using systematic literature reviews in articles enhances the credibility and reliability of the research by providing a structured and rigorous synthesis of existing knowledge. The research includes most of the substances that can lead to psychoses, and it is a comprehensive article that can help to identify these substances conveniently. Psychoactive substances and some medications can cause secondary psychosis. For example, Digitalis, Beta-blockers, Antiarrhythmic in cardiology, Asparaginase, Cytarabine, Fluorouracil, Ifosfamide, Methotrexate, Vincristine in oncology, Dopamine agonists (amantadine, bromocriptine, and levodopa) in neurology, Cimetidine, Ranitidine in gastroenterology and Antidepressants (bupropion, tricyclic antidepressants), Anticholinergics (benztropine, diphenhydramine) in psychiatry can cause secondary psychosis (Table 4).

5. LIMITATIONS AND FUTURE DIRECTIONS

This systematic review has some limitations. There are few scientific research and articles about substance-induced psychoses, and it is difficult to say with certainty that these substances lead to psychoses definitely, and these are all of the substances that may lead to psychoses. First of all, this article has been written about humans, and there is nothing certain about humans, and the effects of substances differ from one another. Secondly, there are lots of substances that are undetermined and uncharted. Also, there will be more human-made substances in the future. Further studies and investigations are required to verify these substances and to find antidotes and cures for substance-induced psychotic patients as well. Finally, this research can only represent the situation of a single part of the whole world population.

CONCLUSION

A few studies indicate that there are a few substances and even medicines that may lead to psychoses with high possibility. Numerous psychological intervention strategies for SIPs show promising treatment results, indicating the potential for customizable interventions that can meet individual needs. It can be concluded that the etiology of psychoses is different. Psychoses can develop because of sad experiences in childhood, available genes, depressing experiences and accidents, some medicines for a long time, or drug misuse. However, the most common reasons are available genes and substances that have been discussed. Unfortunately, these substances change the chemical structures of genes and can lead to other disorders and diseases besides psychoses. However, additional research is needed to effectively put these strategies into practice in interventions that are supported by a reliable mechanism of change and to verify the effectiveness of those interventions.

AUTHORS' CONTRIBUTIONS

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Primary revision: Isaac Karimi

LIST OF ABBREVIATIONS

DSM	=	Diagnostic and Statistical Manual
SIP	=	Substance-induced Psychosis
THC	=	Tetrahydrocannabinol
CBD	=	Cannabidiol
LSD	=	Lysergic Acid Diethylamide

CONSENT FOR PUBLICATION

Not applicable.

STANDARDS OF REPORTING

PRISMA guidelines have been followed.

AVAILABILITY OF DATA AND MATERIALS

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CONFLICT OF INTEREST

Hereby, it has been announced that the authors have no conflict of interest.

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SUPPLEMENTARY MATERIAL

PRISMA checklist is available as supplementary material on the publisher's website along with the published article.

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