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RAISING AWARENESS OF ILLICIT DRUGS IN PAKISTAN, THE ROLE OF SEWAGE WASTEWATER ANALYSIS FOR DRUG DETECTION

Systematic Review

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ABSTRACT

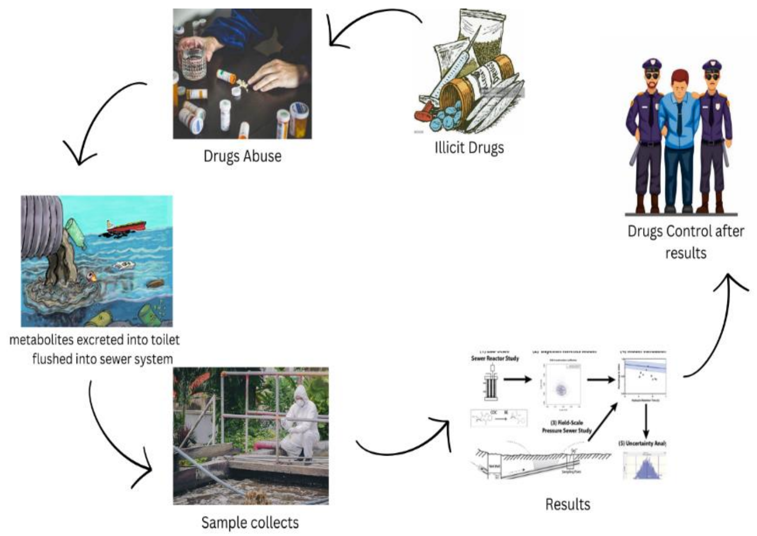
Background: The detection of illicit drugs in sewage water has emerged as a valuable epidemiological tool for assessing community drug consumption patterns. Traditional self-reported surveys often suffer from underreporting and social desirability bias, whereas wastewater-based epidemiology (WBE) provides objective and real-time insights into substance use trends. This method offers a non-invasive and cost-effective approach to understanding drug abuse on a broader scale, aiding public health agencies in developing evidence-based intervention strategies.

Body: A range of advanced analytical techniques, including liquid chromatography-mass spectrometry (LC-MS), gas chromatography-mass spectrometry (GC-MS), high-performance liquid chromatography (HPLC), and immunoassay chromatogram techniques (ICT), are commonly employed to detect drug metabolites in wastewater. These methods enable researchers to estimate overall drug consumption, monitor emerging substance abuse trends, and identify potential public health threats, such as new psychoactive substances and overdose surges. However, despite its advantages, WBE has limitations, including its inability to pinpoint specific sources of drug metabolites or provide individualized consumption data. The ethical considerations of privacy protection and data interpretation remain critical in implementing this methodology responsibly.

Conclusion: Wastewater analysis has significant implications for public health monitoring, drug policy formulation, and law enforcement strategies. By integrating WBE with other epidemiological approaches, policymakers can develop more targeted and effective drug prevention programs. Future research should focus on refining detection methods, addressing ethical concerns, and expanding the application of wastewater analysis to broader public health challenges.

Keywords: Drug abuse monitoring, Forensic toxicology, Illicit drugs, Public health surveillance, Sewage epidemiology, Substance use trends, Wastewater-based epidemiology.

INTRODUCTION



Illicit drug use has emerged as a critical global public health challenge, with profound implications for individuals, families, and societies. These substances, often classified based on their chemical structure, pharmacological effects, and legal status, pose significant risks due to their potential for addiction and adverse health effects (1). Despite stringent legal restrictions, the demand and consumption of illicit drugs continue to escalate, driven by their psychoactive properties that induce euphoria and temporary relief from psychological distress (2). The 21st century has witnessed an alarming rise in the use of substances such as heroin, cocaine, and amphetamine-type stimulants, leading to an expansion of illicit drug markets into a multi-trillion-dollar industry (3). The global burden of drug misuse is reflected in epidemiological data, with illicit substance use contributing to considerable morbidity and mortality. Reports indicate that in 2011, illicit drug consumption accounted for 1.8% of the total disease burden in Australia alone (4). Furthermore, in 2012, over 183,000 deaths were attributed to drug-related causes, with an estimated 243 million cases of substance abuse worldwide (5). The United Nations Office on Drugs and Crime (UNODC) estimated that in 2013, approximately 246 million people engaged in the use of illegal substances (6). These figures continued to rise, as evidenced by the Global Burden of Disease study, which reported 585,000 drug-related deaths in 2017 (7). The impact of illicit drug use extends beyond individual health, exacerbating social instability through increased crime rates, violence, and economic burdens associated with law enforcement and healthcare services (8). Socioeconomically disadvantaged populations are particularly vulnerable, but substance misuse is not confined to any single demographic, affecting individuals across various socioeconomic strata (9).

One of the emerging approaches in forensic and public health research is wastewater-based epidemiology (WBE), a novel technique used to assess drug consumption patterns at the community level (10). This method is based on the detection of drug metabolites in sewage, reflecting the collective drug use of a population. Wastewater analysis has been successfully employed in regions such as Europe, North America, Australia, and parts of Asia to monitor trends in illicit drug use, identify emerging drug threats, and evaluate the effectiveness of public health interventions (11). Its application in public health surveillance provides real-time, objective data that can complement traditional epidemiological methods, offering a cost-effective and non-invasive alternative to individual biological sampling such as blood or urine tests (12). Given Pakistan's increasing concerns regarding drug abuse, the potential application of WBE could offer valuable insights into drug consumption trends, enabling policymakers and healthcare professionals to design targeted interventions. Traditional surveillance methods often rely on self-reported data, which may be influenced by social desirability bias and underreporting. In contrast, wastewater analysis can provide unbiased, population-level estimates, aiding in early detection and response strategies for substance abuse control (13). This review explores the feasibility of utilizing sewage wastewater analysis for drug detection in Pakistan, aiming to bridge the existing knowledge gap and propose a more efficient surveillance framework for illicit drug monitoring. By advancing scientific approaches to drug surveillance, this study seeks to enhance public health efforts, inform law enforcement strategies, and contribute to the broader global discourse on combating illicit drug trafficking and addiction (14).

Table 1: The table contains Narcotic drugs with the Origin of drugs

Narcotic Drugs	Origin of Drugs	References
Cocaine	Derived from coca leaves used by indigenous people in South America	(73)
Opiates	Morphine became widely used as a pain reliever, especially during the American Civil War	(42)

Narcotic Drugs	**Origin of Drugs**	**References**
Alcohol	Mesopotamia Middle East, England, Germany, United States	(99, 135)
Barbiturates	Germany (1912) United States (1923)	(50)
Benzodiazepines	By the fusion of two chemical compound structures benzidine and diazepine	(89)
THC (Cannabinoids)	Cannabis sativa Plant	(122)
MDMA	Germany	(37)
Phencyclidine	Developed as a surgical anaesthetic	(16)
Tramadol	Germany	(5)

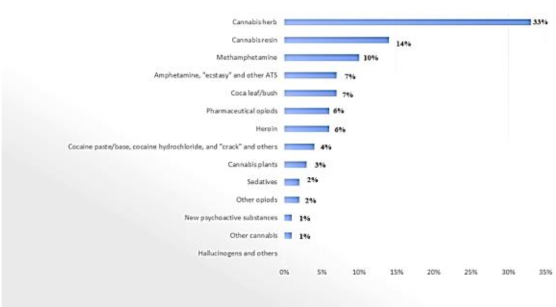


Figure: Global distribution of drug seizure cases by drug types 2019-2020

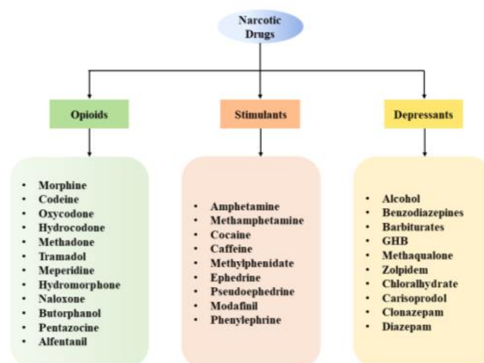


Figure: Visual representation illustrating diverse drug types and their categorization.

Table.2: Table shown overview of Illicit drugs including their discovery, scientist name side effect and function of the drugs.

Drugs	**Discovery**	**Scientist**	**Function**	**Side Effects**	**Reference**
Amphetamines	1887	Lazar Edeleanu	Treat ADHD, narcolepsy, and obesity, stimulant and enhance athletic performance.	Increased heart rate and blood pressure, insomnia, restlessness	(46)
Cocaine	1855	Albert Niemann	Local anesthetic and stimulant	Cardiovascular, respiratory, neurological, psychiatric disorders, and overdose leads to death	(73)
Opiates	~3400 BCE Early 1800s Late 1800s	Sumerians F. Wilhelm Sertürner Bayer	Pain relief cough suppressant	Constipation, respiratory depression	(102)

Alcohol	~7000 BC 10th AD 17th AD 18th AD 19th AD 20th AD	Unknown Jabir bin Hayyan Isaac Newton Johann Joachim Becher	Beverages Medicine Alchemy Chemistry	Liver damage poisoning addiction birth defects	(99, 135)
Barbiturates	1912	Ernst W. von Romberg	Anticonvulsant Sedative hypnotic anesthetic	Sedation, drowsiness, ataxia, addiction, respiratory depression, dizziness confusion	(136,117)
Benzodiazepine	Mid-20th Century	Leo Sternbach	sedatives, anxiolytics, and muscle relaxants	Drowsiness, dizziness, impaired coordination, and addiction.	(70)
Buprenorphine	1966	Brian Lewis	treat opioid addiction and pain management	Constipation, nausea, vomiting, headache, dizziness, and drowsiness. respiratory depression, can occur at higher doses	(120)
Cannabinoids	1964	Raphael Mechoulam	Recreationally, medically for pain, nausea, and appetite stimulation	paranoia, anxiety, dry mouth, increased heart rate, dizziness	(31)
MDMA	1912	Anton Köllisch	control bleeding, increase empathy, treat PTSD	dehydration, hyperthermia, hypertension, and heart failure	(141)
Methadone	1937	Max Bockmühl.	used for the treatment of opioid, reduce withdrawal symptoms and cravings	Drowsiness, dizziness, Nausea, constipation, sweating and respiratory depression	(54)
Phencyclidine	1956	Victor Maddox	Originally used as a surgical anesthetic, but later abused as a recreational drug	Hallucinations, dissociative states, psychosis, agitation, violence, elevated blood pressure, rapid heart rate, and muscle rigidity	(62)
Tramadol	1962	Kurt Flick and Helmut Bein.	used to treat moderate to severe pain	Nausea, dizziness, constipation, seizures and serotonin syndrome	(125)

MAIN BODY

Methods of Illicit Drug Detection from Sewage Water

The detection of illicit drugs in sewage water has become an innovative and effective approach to understanding drug consumption patterns in a given population. This method, widely used in forensic science and public health surveillance, involves analyzing wastewater samples for the presence of drug metabolites, thereby providing real-time insights into substance use trends at a community level (1). By bypassing the limitations of self-reported surveys and biological testing, wastewater-based epidemiology (WBE) has proven to be a cost-effective, non-invasive, and scalable technique for estimating drug use on a large scale (2). This section outlines the methodologies involved in detecting illicit drugs in sewage water, including sample collection, analytical techniques, and data analysis.

Wastewater-Based Epidemiology (WBE) for Drug Detection

WBE is a well-established method used to assess the concentration of illicit drugs and their metabolites in wastewater, reflecting collective drug use patterns within a population (3). By analyzing influent sewage from wastewater treatment plants (WWTPs), researchers can quantify drug consumption trends, identify emerging substances, and evaluate the impact of drug policies or public health interventions (4). This methodology has been successfully implemented in Europe, North America, and Asia, demonstrating its effectiveness in monitoring illicit drug use and informing law enforcement and public health authorities (5).

The detection process follows a systematic approach involving three primary stages:

Sample Collection

Wastewater samples are collected from WWTPs, specifically at influent points where raw sewage enters the treatment facility (6). Samples may also be obtained from sewer networks, particularly in areas of interest such as high-risk zones or specific neighborhoods (7). Collection methods include manual grab sampling, where individual samples are taken at specific times, and composite sampling, which aggregates samples over a set duration to provide a more representative analysis (8). Automated sampling systems are preferred in large-scale studies to ensure consistency and accuracy in data collection (9).

Analytical Techniques for Drug Detection

The presence of illicit drugs and their metabolites in wastewater is determined through advanced chemical and analytical techniques. These methods offer high sensitivity and specificity, enabling the detection of trace amounts of substances with minimal interference. The two primary analytical techniques used in wastewater analysis are Liquid Chromatography-Mass Spectrometry (LC-MS) and Gas Chromatography-Mass Spectrometry (GC-MS) (10).

Liquid Chromatography-Mass Spectrometry (LC-MS)

LC-MS is a powerful technique used to identify and quantify drug compounds in wastewater. It involves the separation of drug metabolites via liquid chromatography, followed by mass spectrometric detection based on molecular weight and structure (11). The key steps in LC-MS analysis include:

- Sample Preparation: Wastewater samples undergo filtration, extraction, and purification to remove contaminants and concentrate the target analytes (12).
- Chromatographic Separation: The processed sample is introduced into the liquid chromatography system, where components are separated based on their chemical properties (13).
- Ionization and Mass Analysis: The separated compounds enter the mass spectrometer, where they are ionized and analyzed based on their mass-to-charge (m/z) ratio (14).
- Data Processing: The detected ions are matched with known drug metabolites in reference databases to confirm their identity and concentration (15).

Gas Chromatography-Mass Spectrometry (GC-MS)

GC-MS is another widely used technique for the analysis of volatile and semi-volatile drug compounds in wastewater (16). Unlike LC-MS, which is better suited for polar compounds, GC-MS is particularly effective for detecting stimulant drugs such as methamphetamine and cocaine. The process follows similar steps:

- Sample Extraction: Target analytes are isolated using liquid-liquid extraction or solid-phase extraction techniques (17).
- Chromatographic Separation: The extracted sample is introduced into the gas chromatograph, where compounds are vaporized and separated based on their chemical properties (18).
- Mass Spectrometric Detection: The separated compounds are ionized, fragmented, and analyzed to generate a unique mass spectrum for each drug metabolite (19).
- Quantification and Interpretation: The detected substances are compared against standard reference spectra to determine their concentration and prevalence in the wastewater sample (20).

Data Analysis and Interpretation

Once drug metabolites are quantified, the results are analyzed to estimate drug consumption levels and trends within the community. This process involves:

- Back-Calculation of Drug Use: By applying established pharmacokinetic models, researchers estimate the amount of drugs consumed in the population based on the concentration of metabolites detected in wastewater (21).
- Trend Analysis: Continuous monitoring allows for the detection of seasonal or geographical variations in drug use, providing insights into substance use behaviors over time (22).
- Correlation with Public Health Data: Wastewater findings are compared with epidemiological data, such as hospital admissions and overdose reports, to validate trends and inform policy decisions (23).

Enzyme-Linked Immunosorbent Assay (ELISA) for Drug Detection

In addition to LC-MS and GC-MS, the Enzyme-Linked Immunosorbent Assay (ELISA) is used as a rapid screening method for drug detection in wastewater. ELISA relies on antigen-antibody interactions to identify specific drug compounds based on their unique molecular structures (24). This technique offers several advantages, including high sensitivity, cost-effectiveness, and the ability to detect a broad range of illicit drugs (25). However, it is often used as a preliminary screening tool, with positive findings requiring confirmation via more precise methods such as LC-MS or GC-MS (26).

The ELISA process follows a structured approach:

- Sample Collection and Preparation: Wastewater samples are collected and treated with reagents to isolate drug molecules (27).
- Antibody Binding and Detection: Specific antibodies are introduced, binding to drug metabolites and triggering a detectable enzymatic reaction (28).
- Quantification of Drug Presence: The intensity of the enzymatic signal correlates with the concentration of the drug in the sample, allowing for semi-quantitative analysis (29).

While ELISA is useful for rapid screening, its limitations include the potential for cross-reactivity with structurally similar compounds, leading to false positives (30). Therefore, it is commonly employed in conjunction with mass spectrometry techniques for comprehensive drug surveillance.

Risk of Drugs to Society

Illicit drug use presents a profound public health and social challenge, significantly impacting individuals, families, and communities worldwide. The consequences of drug abuse extend beyond the immediate physical and psychological health risks, contributing to social instability, criminal activities, economic losses, and a burden on healthcare systems (1). A substantial body of research has linked drug consumption to a myriad of health complications, economic burdens, and societal dysfunctions, necessitating comprehensive strategies to mitigate its effects.

Health Risks Associated with Drug Use

The physical and psychological consequences of drug use are well-documented, with studies indicating a strong association between substance abuse and chronic health conditions. Long-term consumption of drugs such as cocaine, methamphetamine, and marijuana has been shown to elevate the risk of cardiovascular diseases, strokes, respiratory disorders, and liver dysfunctions (2). Opioid use, particularly through injection, increases susceptibility to infections such as hepatitis and HIV, contributing to long-term morbidity and mortality (3). In addition to physical health risks, substance use is strongly correlated with mental health disorders. Anxiety, depression, and psychosis are commonly reported among drug users, with certain substances directly impacting neurological pathways and cognitive functions (4). Methamphetamine, for instance, has been extensively linked to psychotic episodes, while prolonged exposure to cannabinoids can induce psychosis, cognitive impairment, and altered perception (5). Tobacco use has also been associated with subclinical psychotic symptoms in the general population, further emphasizing the link between drug consumption and mental health disorders (6). The need for a multi-faceted public health approach is evident, incorporating harm reduction strategies, preventive interventions, and treatment programs. Initiatives such as naloxone distribution, drug testing services, and safe injection facilities have been proposed as effective measures to reduce the adverse health consequences of drug use while promoting education and outreach programs (7).

Criminal and Social Consequences of Drug Use

The illicit drug trade is intrinsically linked to criminal activity, fueling violence, corruption, and social unrest. The illegal drug economy is often associated with organized crime networks engaged in drug trafficking, money laundering, theft, and even homicide, creating security threats at both national and international levels (8). The impacts of drug-related crime extend beyond direct violence, affecting political stability, law enforcement efficiency, and community safety (9). The global nature of drug trade exacerbates these risks, with trafficking routes spanning multiple continents and facilitating the proliferation of illicit substances worldwide. Individuals involved in drug consumption or distribution frequently engage in criminal behavior to sustain their habits, increasing the risk of incarceration and legal consequences (10). However, punitive measures alone have proven insufficient in addressing the complexities of drug-related crime. A growing consensus among policymakers and researchers suggests that integrated strategies, combining law enforcement with rehabilitation programs and harm reduction approaches, may yield more effective results in curbing drug-related offenses (11).

The economic burden of illicit drug use is another pressing concern. The financial toll of substance abuse is reflected in healthcare expenditures, lost productivity, and law enforcement costs. In the United States, drug-related economic losses were estimated at $740 billion in 2019, encompassing direct healthcare costs, criminal justice expenditures, and productivity losses (12). These expenses are borne by taxpayers and society at large, highlighting the need for targeted interventions that address both the supply and demand aspects of drug consumption. Substance abuse in the workplace further exacerbates economic losses, contributing to absenteeism, reduced efficiency, and high turnover rates (13). Employers face significant challenges in managing drug-related workplace issues, with studies indicating that substance abuse is a major contributor to occupational injuries and diminished workforce productivity (14). Healthcare costs associated with drug abuse, including emergency room visits, hospital admissions, and long-term rehabilitation services, further strain public health resources, underscoring the need for preventive strategies and early intervention programs (15).

Public Health Implications and Disease Transmission

Injectable drug use presents a significant risk for the transmission of infectious diseases, particularly HIV and hepatitis C. Studies indicate that needle-sharing practices among drug users are a leading cause of new infections, exacerbating public health challenges in many countries (16). The World Health Organization (WHO) reported that in 2019, approximately 1.7 million new HIV infections occurred globally, with a significant proportion attributed to injection drug use (17). Overdose fatalities have also risen at an alarming rate, particularly with the increased availability of synthetic opioids such as fentanyl. In the United States, over 93,000 drug overdose deaths were recorded in 2020, marking the highest number ever reported (18). Similarly, in Canada, opioid-related deaths have surged in recent years, with more than 17,000 fatalities recorded between 2016 and 2020 (19). These statistics underscore the urgency of implementing harm reduction policies, including supervised injection facilities, overdose prevention programs, and access to addiction treatment services (20).

Distribution of Drugs and Global Drug Trafficking

The global illicit drug market continues to expand, with drug trafficking networks evolving to meet increasing demand. The United Nations Office on Drugs and Crime (UNODC) estimated that in 2018, the global drug trade was valued at approximately $500 billion, making it one of the most lucrative illicit industries (21). The production and distribution of narcotics, including cocaine, heroin, and synthetic opioids, remain major concerns, particularly in regions with weak law enforcement and high drug demand. Cocaine production, for example, reached a record high of 1,976 tonnes in 2019, with Colombia and Peru being the primary producers (22). Similarly, the synthetic drug market has grown exponentially, with China and Myanmar emerging as significant producers of fentanyl and methamphetamine (23). The expansion of dark web markets and advanced smuggling techniques have further complicated law enforcement efforts, necessitating enhanced international cooperation and intelligence-sharing mechanisms (24). At the local level, drug distribution patterns vary based on economic, social, and geographical factors. Urban centers with high crime rates often serve as hubs for drug trade, contributing to increased violence and social disruption. Community-based interventions, law enforcement crackdowns, and public awareness campaigns are critical in addressing local drug markets and reducing accessibility to illicit substances (25).

Awareness of Drug Addiction in Pakistan

Pakistan has witnessed a significant rise in drug addiction, with an estimated 7.6 million individuals affected, making it one of the countries with the highest drug consumption rates globally (26). Cannabis, heroin, and prescription medications are among the most commonly abused substances, with heroin addiction being particularly prevalent due to Pakistan's proximity to Afghanistan, a major opium producer (27). Despite efforts to curb drug abuse, stigma and lack of awareness remain major barriers to effective intervention. Many individuals struggling with addiction avoid seeking help due to societal judgment and inadequate treatment resources. In response, the Pakistani government has implemented measures such as the establishment of de-addiction centers, public awareness campaigns, and the Anti-Narcotics Force (ANF) to combat drug trafficking (28). However, these initiatives require further strengthening through community engagement, educational programs, and expanded treatment facilities. Raising awareness about drug addiction is essential in mitigating its impact. Strategies such as government-led public service campaigns, school-based education programs, peer-to-peer initiatives, media involvement, and improved rehabilitation services can play a crucial role in addressing substance abuse in Pakistan (29). By fostering a more informed and supportive society, individuals struggling with addiction may be more likely to seek help, reducing the long-term consequences of drug abuse.

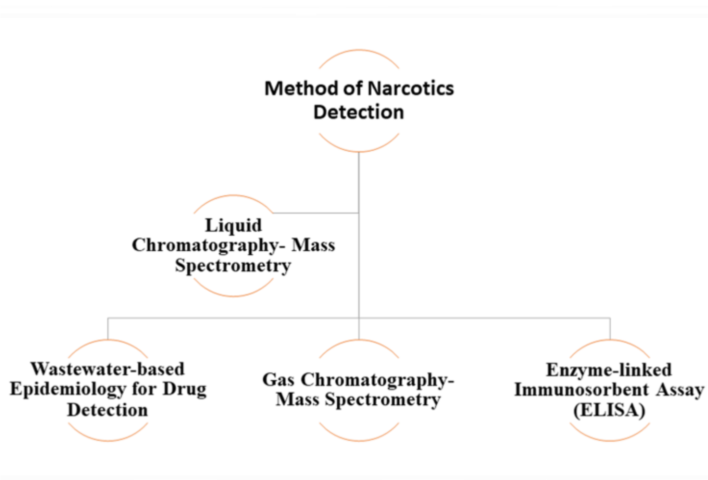


Figure: Techniques that is used for Illicit drugs detection.

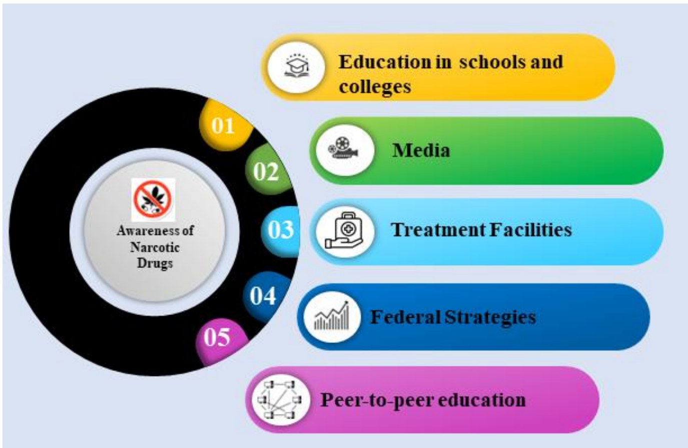


Figure: This figure illustrates the promotion of awareness on drug addiction in Pakistan

Figure: Diagrammatic representation illustrating the societal risks associated with drug use.

CONCLUSION

The analysis of illicit drugs in sewage water presents a valuable tool for understanding community-level drug consumption patterns, offering insights that can inform public health interventions and policy measures. By examining wastewater, researchers can identify prevalent substances, detect emerging drug trends, and assess the effectiveness of substance abuse prevention programs. However, this approach does not track individual drug use, emphasizing its role in broader epidemiological surveillance rather than personal monitoring. Ethical considerations, including privacy protections and responsible data interpretation, remain paramount in implementing wastewater-based drug detection strategies. While this method enhances public health efforts, its efficacy is maximized when integrated with complementary research methodologies, such as clinical studies and sociological surveys, to provide a comprehensive understanding of substance use trends. Moving forward, raising public awareness, strengthening harm reduction programs, and refining policy frameworks will be crucial in addressing drug-related challenges effectively.

AUTHOR CONTRIBUTIONS

Author	Contribution
Ubaid Ullah Khan*	Substantial Contribution to study design, analysis, acquisition of Data Manuscript Writing Has given Final Approval of the version to be published
Maham Noor	Substantial Contribution to study design, acquisition and interpretation of Data Critical Review and Manuscript Writing Has given Final Approval of the version to be published
Sajid Hussain	Substantial Contribution to acquisition and interpretation of Data Has given Final Approval of the version to be published
Mehreen Ishtiaq	Contributed to Data Collection and Analysis Has given Final Approval of the version to be published
Inam Ullah	Contributed to Data Collection and Analysis Has given Final Approval of the version to be published
Zeeshan Abbas	Substantial Contribution to study design and Data Analysis Has given Final Approval of the version to be published
Haseeb Ullah	Contributed to study concept and Data collection Has given Final Approval of the version to be published
Rehan Jamal	Writing - Review & Editing, Assistance with Data Curation
Abdul Wahab	Writing - Review & Editing, Assistance with Data Curation

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