The Organic Chemistry of Drugs

Chandresh Pareek
Associate Professor in Chemistry, JDB Govt. Girls College, Kota, Rajasthan, India

Sule Korkmaz
Research Scholar at Istanbul University, Istanbul, Turkey

Jagrit Pareek
Research Scholar at BITS Pilani, Rajasthan, India

Narendra Nirwan
Assistant Professor in Chemistry, Govt. College, Ajmer, Rajasthan, India

Annotation: In pharmacology, a drug is a chemical substance, typically of known structure, which, when administered to a living organism, produces a biological effect. A pharmaceutical drug, also called a medication or medicine, is a chemical substance used to treat, cure, prevent, or diagnose a disease or to promote well-being. Traditionally drugs were obtained through extraction from medicinal plants, but more recently also by organic synthesis. While there are several types of exceptions, the effects of most drugs result from their interaction with functional macromolecular components of the organism. Such interaction alters the function of the pertinent cellular component and thereby initiates the series of biochemical and physiological changes that are characteristic of the response to the drug. The term receptor is used to denote the component of the organism with which the chemical agent interacts.

Keywords: drug, medication, disease, biochemical, receptor, organic, synthesis, biochemical, physiological.

Introduction
A drug is any chemical substance that causes a change in an organism's physiology or psychology when consumed.[1][2] Drugs are typically distinguished from food and substances that provide nutritional support. Consumption of drugs can be via inhalation, injection, smoking, ingestion, absorption via a patch on the skin, suppository, or dissolution under the tongue. In pharmacology, a drug is a chemical substance, typically of known structure, which, when administered to a living organism, produces a biological effect.[3] A pharmaceutical drug, also called a medication or medicine, is a chemical substance used to treat, cure, prevent, or diagnose a disease or to promote well-being.[1] Traditionally drugs were obtained through extraction from medicinal plants, but more recently also by organic synthesis.[4] Pharmaceutical drugs may be used for a limited duration, or on a regular basis for chronic disorders.[5] Pharmaceutical drugs are often classified into drug classes—groups of related drugs that have similar chemical structures, the same mechanism of action (binding to the same biological target), a related mode of action, and that are used to treat the same disease.[6][7] The Anatomical Therapeutic Chemical Classification System (ATC), the most widely used drug classification system, assigns drugs a unique ATC code, which is an alphanumeric code that assigns it to specific drug classes within the ATC system. Another major classification system is the Bio pharmaceuticals Classification System. This classifies drugs according to their solubility and permeability or absorption properties.[8] Psychoactive drugs are chemical substances that affect the function of the central nervous system, altering perception, mood or consciousness.[9] These drugs are divided into different groups like: stimulants, depressants, antidepressants, anxiolytics, antipsychotics, and hallucinogens. These psychoactive drugs have been proven useful in treating a wide range of medical conditions including mental...
disorders around the world. The most widely used drugs in the world include caffeine, nicotine and alcohol,[10] which are also considered recreational drugs, since they are used for pleasure rather than medicinal purposes.[11] All drugs can have potential side effects.[12] Abuse of several psychoactive drugs can cause addiction and/or physical dependence.[13] Excessive use of stimulants can promote stimulant psychosis. Many recreational drugs are illicit and international treaties such as the Single Convention on Narcotic Drugs exist for the purpose of their prohibition.

A medication or medicine is a drug taken to cure or ameliorate any symptoms of an illness or medical condition. [14] The use may also be as preventive medicine that has future benefits but does not treat any existing or pre-existing diseases or symptoms. Dispensing of medication is often regulated by governments into three categories—over-the-counter medications, which are available in pharmacies and supermarkets without special restrictions;[15] behind-the-counter medicines, which are dispensed by a pharmacist without needing a doctor's prescription, and prescription only medicines, which must be prescribed by a licensed medical professional, usually a physician.[19] In the United Kingdom, behind-the-counter medicines are called pharmacy medicines which can only be sold in registered pharmacies, by or under the supervision of a pharmacist. These medications are designated by the letter P on the label.[20] The range of medicines available without a prescription[16][17][18] varies from country to country. Medications are typically produced by pharmaceutical companies and are often patented to give the developer exclusive rights to produce them. Those that are not patented (or with expired patents) are called generic drugs since they can be produced by other companies without restrictions or licenses from the patent holder.[21] Pharmaceutical drugs are usually categorised into drug classes. A group of drugs will share a similar chemical structure, or have the same mechanism of action, the same related mode of action or target the same illness or related illnesses.[6][7] The Anatomical Therapeutic Chemical Classification System (ATC), the most widely used drug classification system, assigns drugs a unique ATC code, which is an alphanumeric code that assigns[22][23][24] it to specific drug classes within the ATC system. Another major classification system is the Bio pharmaceutics Classification System. This groups drugs according to their solubility and permeability or absorption properties.[8]

Discussion

Club drugs, also called rave drugs or party drugs, are a loosely defined category of recreational drugs which are associated with discothèques in the 1970s and nightclubs, dance clubs, electronic dance music (EDM) parties, and raves in the 1980s to today.[1][2][3] Unlike many other categories, such as opiates and benzodiazepines, which are established according to pharmaceutical or chemical properties, club drugs are a "category of convenience", in which drugs are included due to the locations they are consumed and/or where the user goes while under the influence of the drugs.[25][26] Club drugs are generally used by adolescents and young adults.[2][4] This group of drugs is also called "designer drugs", as most are synthesized in a chemical lab (e.g., MDMA, ketamine, LSD) rather than being sourced from plants (as with marijuana, which comes from the cannabis plant) or opiates (which are naturally derived from the opium poppy).[5] Club drugs range from entactogens such as MDMA ("ecstasy"), 2C-B ("nexus") and inhalants (e.g., nitrous oxide and poppers) to stimulants (e.g., amphetamine and cocaine), depressants/sedatives (Quaaludes, GHB, Rohypnol) and psychedelic and hallucinogenic drugs (LSD, magic mushrooms and DMT). Dancers at all-night parties and dance events have used some of these drugs for their stimulating properties since the 1960s Mod subculture in U.K.,[27][28][29] whose members took amphetamine to stay up all night. In the 1970s disco scene, the club drugs of choice shifted to the stimulant cocaine and the depressant Quaaludes. Quaaludes were so common at disco clubs that the drug was nicknamed "disco biscuits". In the 1990s and 2000s, methamphetamine and MDMA are sold and used in many clubs. "Club drugs" [30][31]vary by country and region; in some regions, even opiates such as heroin and morphine have been sold at clubs, though this practice is relatively uncommon.[6] Narconon states that other synthetic drugs used in clubs, or which are sold
as "Ecstasy", include harmaline; piperazines (e.g., BZP and TFMPP); PMA/PMMA; mephedrone (generally used outside the US) and MDPV.[7] The legal status of club drugs varies according to the region and the drug. Some drugs are legal in some jurisdictions, such as "poppers" (which are often sold as "room deodorizer" or "leather polish" to get around drug laws) and nitrous oxide (which is legal when used from a whipped cream can). Other club drugs, such as amphetamine, are generally illegal unless the individual has a medical prescription.[32][33] Some club drugs are almost always illegal, such as cocaine and MDMA. There are a range of risks from using club drugs. As with all drugs, from legal drugs like alcohol to illegal drugs like BZP, usage can increase the risk of injury due to falls, dangerous or risky behavior (e.g., unsafe sex) and, if the user drives, injury or death due to impaired driving accidents. Some club drugs, such as cocaine and amphetamines, are addictive, and regular use can lead to the user craving more of the drug. Some club drugs are more associated with overdoses. Some club drugs can cause adverse health effects which can be harmful to the user, such as the dehydration associated with MDMA use in an all-night dance club setting.[8]

Some religions, particularly ethnic religions, are based completely on the use of certain drugs, known as entheogens, which are mostly hallucinogens,—psychedelics, dissociatives, or deliriants. Some drugs used as entheogens include kava which can act as a stimulant, a sedative, an euphoriant and an anesthetic. The roots of the kava plant are used to produce a drink which is consumed throughout the cultures of the Pacific Ocean. Some shamans from different cultures use entheogens, defined as "generating the divine within"[22] to achieve religious ecstasy. Amazonian shamans use ayahuasca (yagé) a hallucinogenic brew for this purpose. Mazatec shamans have a long and continuous tradition of religious use of Salvia divinorum a psychoactive plant. Its use is to facilitate visionary states of consciousness during spiritual healing sessions.[23] Silene undulata is regarded by the Xhosa people as a sacred plant and used as an entheogen. Its roots are traditionally used to induce vivid (and according to the Xhosa, prophetic) lucid dreams during the initiation process of shamans, classifying it a naturally occurring oneirogen similar to the more well-known dream herb Calea ternifolia.[24] Peyote, a small spineless cactus, has been a major source of psychedelic mescaline and has probably been used by Native Americans[34][35] for at least five thousand years.[25][26] Most mescaline is now obtained from a few species of columnar cacti in particular from San Pedro and not from the vulnerable peyote.[27] The entheogenic use of cannabis has also been widely practised[28] for centuries.[29] Rastafari use marijuana (ganja) as a sacrament in their religious ceremonies. Psychedelic mushrooms (psilocybin mushrooms), commonly called magic mushrooms or shrooms have also long been used as entheogens.[36]

Nootropics, also commonly referred to as "smart drugs", are drugs that are claimed to improve human cognitive abilities.[37] Nootropics are used to improve memory, concentration, thought, mood, and learning. An increasingly used nootropic among students, also known as a study drug, is methylphenidate branded commonly as Ritalin and used for the treatment of attention deficit hyperactivity disorder (ADHD) and narcolepsy.[30] At high doses methylphenidate can become highly addictive.[31] Serious addiction can lead to psychosis, anxiety and heart problems, and the use of this drug is related to a rise in suicides, and overdoses. Evidence for use outside of student settings is limited but suggests that it is commonplace.[30][31] Intravenous use of methylphenidate can lead to emphysematous damage to the lungs, known as Ritalin lung.[32]

Other drugs known as designer drugs are produced. An early example of what today would be labelled a 'designer drug' was LSD, which was synthesised from ergot.[33] Other examples include analogs of performance-enhancing drugs such as designer steroids taken to improve physical capabilities and these are sometimes used (legally or not) for this purpose, often by professional athletes.[34] Other designer drugs mimic the effects of psychoactive drugs. Since the late 1990s there has been the identification of many of these synthesised drugs. In Japan and the United Kingdom this has spurred the addition of many designer drugs into a newer class of controlled substances...
known as a temporary class drug.[38] Synthetic cannabinoids have been produced for a longer period of time and are used in the designer drug synthetic cannabis.[39]

Results

Drug development is the process of bringing a new pharmaceutical drug to the market once a lead compound has been identified through the process of drug discovery. It includes preclinical research on microorganisms and animals, filing for regulatory status, such as via the United States Food and Drug Administration for an investigational new drug to initiate clinical trials on humans, and may include the step of obtaining regulatory approval with a new drug application to market the drug.[1][2] The entire process – from concept through preclinical testing in the laboratory to clinical trial development, including Phase I–III trials – to approved vaccine or drug typically takes more than a decade. New chemical entities (NCEs, also known as new molecular entities or NMEs) are compounds that emerge from the process of drug discovery. These have promising activity against a particular biological target that is important in disease. However, little is known about the safety, toxicity, pharmacokinetics, and metabolism of this NCE in humans. [40] It is the function of drug development to assess all of these parameters prior to human clinical trials. A further major objective of drug development is to recommend the dose and schedule for the first use in a human clinical trial ("first-in-human" [FIH] or First Human Dose [FHD], previously also known as "first-in-man" [FIM]). In addition, drug development must establish the physicochemical properties of the NCE: its chemical makeup, stability, and solubility. Manufacturers must optimize the process they use to make the chemical so they can scale up from a medicinal chemist producing milligrams, to manufacturing on the kilogram and ton scale. They further examine the product for suitability to package as capsules, tablets, aerosol, intramuscular injectable, subcutaneous injectable, or intravenous formulations. Together, these processes are known in preclinical and clinical development as chemistry, manufacturing, and control (CMC). Many aspects of drug development focus on satisfying the regulatory requirements for a new drug application. These generally constitute a number of tests designed to determine the major toxicities of a novel compound prior to first use in humans. It is a legal requirement that an assessment of major organ toxicity be performed (effects on the heart and lungs, brain, kidney, liver and digestive system), as well as effects on other parts of the body that might be affected by the drug (e.g., the skin if the new drug is to be delivered on or through the skin). Such preliminary tests are made using in vitro methods (e.g., with isolated cells), but many tests can only use experimental animals to demonstrate the complex interplay of metabolism and drug exposure on toxicity.[6] The information is gathered from this preclinical testing, as well as information on CMC, and submitted to regulatory authorities (in the US, to the FDA), as an Investigational New Drug (IND) application. If the IND is approved, development moves to the clinical phase.[41]

Recreational drug use is the use of a drug (legal, controlled, or illegal) with the primary intention of altering the state of consciousness through alteration of the central nervous system in order to create positive emotions and feelings. The hallucinogen LSD is a psychoactive drug commonly used as a recreational drug.[36] Ketamine is a drug used for anesthesia, and is also used as a recreational drug, both in powder and liquid form, for its hallucinogenic and dissociative effects.[37] Some national laws prohibit the use of different recreational drugs; and medicinal drugs that have the potential for recreational use are often heavily regulated. However, there are many recreational drugs that are legal in many jurisdictions and widely culturally accepted. Cannabis is the most commonly consumed controlled recreational drug in the world (as of 2012).[38] Its use in many countries is illegal but is legally used in several countries usually with the proviso that it can only be used for personal use. It can be used in the leaf form of marijuana (grass), or in the resin form of hashish. Marijuana is a more mild form of cannabis than hashish. There may be an age restriction on the consumption and purchase of legal recreational drugs. Some recreational drugs that are legal and accepted in many places include alcohol, tobacco, betel nut, and caffeine products, and in some areas of the world the legal use of drugs such as khat is common.[39] There are a
number of legal intoxicants commonly called legal highs that are used recreationally. The most widely used of these is alcohol.

All drugs, can be administered via a number of routes, and many can be administered by more than one. Bolus is the administration of a medication, drug or other compound that is given to raise its concentration in blood to an effective level. The administration can be given intravenously, by parenteral, by indovenous, by intramuscular, intrathecal or subcutaneous injection. Inhaled, (breathed into the lungs), as an aerosol, inhaler, vape or dry powder (this includes smoking or vaping a substance). Injection as a solution, suspension or emulsion either: intramuscular, intravenous, intraperitoneal, intraoesous. Insufflation, as a nasal spray or snorting into the nose. Orally, as a liquid or solid, that is absorbed through the intestines. Rectally as a suppository, that is absorbed by the rectum or colon. Sublingually, diffusing into the blood through tissues under the tongue. Topically, usually as a cream or ointment. A drug administered in this manner may be given to act locally or systemically. Vaginally as a pessary, primarily to treat vaginal infections.[40]

Clinical trials involve three or four steps:[7]

Phase I trials, usually in healthy volunteers, determine safety and dosing. Phase II trials are used to get an initial reading of efficacy and further explore safety in small numbers of patients having the disease targeted by the NCE. Phase III trials are large, pivotal trials to determine safety and efficacy in sufficiently large numbers of patients with the targeted disease. If safety and efficacy are adequately proved, clinical testing may stop at this step and the NCE advances to the new drug application (NDA) stage. Phase IV trials are post-approval trials that are sometimes a condition attached by the FDA, also called post-market surveillance studies. The process of defining characteristics of the drug does not stop once an NCE is advanced into human clinical trials. In addition to the tests required to move a novel vaccine or antiviral drug into the clinic for the first time, manufacturers must ensure that any long-term or chronic toxicities are well-defined, including effects on systems not previously monitored (fertility, reproduction, immune system, among others).[8][9] If a vaccine candidate or antiviral compound emerges from these tests with an acceptable toxicity and safety profile, and the manufacturer can further show it has the desired effect in clinical trials, then the NCE portfolio of evidence can be submitted for marketing approval in the various countries where the manufacturer plans to sell it.[4] In the United States, this process is called a "new drug application" or NDA.[4][8]

Most novel drug candidates (NCEs) fail during drug development, either because they have unacceptable toxicity or because they simply do not prove efficacy on the targeted disease, as shown in Phase II–III clinical trials.[4][8] Critical reviews of drug development programs indicate that Phase II–III clinical trials fail due mainly to unknown toxic side effects (50% failure of Phase II cardiology trials), and because of inadequate financing, trial design weaknesses, or poor trial execution.[10][11] A study covering clinical research in the 1980–90s found that only 21.5% of drug candidates that started Phase I trials were eventually approved for marketing.[12] During 2006–15, the success rate of obtaining approval from Phase I to successful Phase III trials was under 10% on average, and 16% specifically for vaccines.[13] The high failure rates associated with pharmaceutical development are referred to as an "attrition rate", requiring decisions during the early stages of drug development to "kill" projects early to avoid costly failures.[13][14] One 2010 study assessed both capitalized and out-of-pocket costs for bringing a single new drug to market was about US$1.8 billion and $870 million, respectively.[15] A median cost estimate of 2015–16 trials for development of 10 anti-cancer drugs was $648 million.[16] In 2017, the median cost of a pivotal trial across all clinical indications was $19 million.[17] The average cost (2013 dollars) of each stage of clinical research was US$25 million for a Phase I safety study, $59 million for a Phase II randomized controlled efficacy study, and $255 million for a pivotal Phase III trial to demonstrate its equivalence or superiority to an existing approved drug.[18] Possibly as high as $345 million.[17] The average cost of conducting a 2015–16 pivotal Phase III trial on an infectious disease drug candidate was $22 million.[17] The full cost of bringing a new
drug (i.e., new chemical entity) to market – from discovery through clinical trials to approval – is complex and controversial.[8][19][17][20] In a 2016 review of 106 drug candidates assessed through clinical trials, the total capital expenditure for a manufacturer having a drug approved through successful Phase III trials was $2.6 billion (in 2013 dollars), an amount increasing at an annual rate of 8.5%.[18] Over 2003–2013 for companies that approved 8–13 drugs, the cost per drug could rise to as high as $5.5 billion, due mainly to international geographic expansion for marketing and ongoing costs for Phase IV trials for continuous safety surveillance.[21] Alternatives to conventional drug development have the objective for universities, governments, and the pharmaceutical industry to collaborate and optimize resources.[22] An example of a collaborative drug development initiative is COVID Moonshot, an international open-science project started in March 2020 with the goal of developing an unpatented oral antiviral drug to treat SARS-CoV-2.[23][24]

Conclusions

There are numerous governmental offices in many countries that deal with the control and oversee of drug manufacture and use, and the implementation of various drug laws. The Single Convention on Narcotic Drugs is an international treaty brought about in 1961 to prohibit the use of narcotics save for those used in medical research and treatment. In 1971, a second treaty the Convention on Psychotropic Substances had to be introduced to deal with newer recreational psychoactive and psychedelic drugs. The legal status of *Salvia divinorum* varies in many countries and even in states within the United States. Where it is legislated against the degree of prohibition also varies.[40]The Food and Drug Administration (FDA) in the United States is a federal agency responsible for protecting and promoting public health through the regulation and supervision of food safety, tobacco products, dietary supplements, prescription and over-the-counter medications, vaccines, biopharmaceuticals, blood transfusions, medical devices, electromagnetic radiation emitting devices, cosmetics, animal foods and veterinary drugs. In India, the Narcotics Control Bureau (abbr. NCB), an Indian federal law enforcement and intelligence agency under the Ministry of Home Affairs, Government of India is tasked with combating drug trafficking and assisting international use of illegal substances under the provisions of Narcotic Drugs and Psychotropic Substances Act.[41][42]

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