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Drug discovery and development: current practices and future

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Abstract

Drug discovery and development encompasses the entire procedure of recognizing a drug from its discovery phase until its launch to market. The field of drug design discovery and development is a multifaceted, high-risk, high octane, and probably highly illuminating and rewarding venture. The current study aimed to highlight the current practices and future of drug discovery and development. Various databases, including Scopus, Web of Science, and PubMed, were utilized to search the literature. Natural products are still the first choice of starting material for drug discovery despite recent advances, the rise, and the integral role of combinatorial chemistry in the lead discovery process. Recent analytical and computer technology developments have opened new avenues for processing complex natural products and using their structures to generate new and innovative drugs. In recent times, it has promised biotechnology as a forerunner in the path to the insurrection of human lives. Various products include novel vaccines, diagnostic devices, and new therapeutic strategies, are the achievements of biotechnology in the biomedical domain. Drug discovery is a multidimensional question. It must be evaluated during drug candidates' selection by several parameters such as safety, pharmacokinetics, and efficacy. For a drug entity to pass different stages of its development has to go through significant drawbacks and pitfalls.

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Introduction

Drug discovery is an innovative practice of discovering and identifying new drug entities and medicines. The process is carried out through knowledge and practice of various disciplines such as pharmacology, chemistry, and biology. Drug discovery and development encompasses the entire procedure of recognizing a drug from its discovery phase until its launch to market. The process might comprise series of steps involving potent drug identification through screening of combinatorial chemical libraries or from natural products or drug designing thorough understanding of drug targeting (Thomford *et al.,* 2018). The development phase involves various animal and microbial investigations and animal and human clinical trials, which all converge to the ultimate regulatory approval from concerned federal organizations. Currently, the pharmaceutical industry faces besiegement through strict perusal by the general public, the financial community, and different regulators. Consequently, the progression in drug discovery and new drug approvals is now showing a downward trend from the last decade. Furthermore, this scrutiny put by various groups mentioned earlier poses a big question mark on the safety of highly successful existing drugs (van der Greef and McBurney, 2005).

The field of drug design discovery and development is a multifaceted, high-risk, high octane, and probably highly illuminating and rewarding venture. Corporations involved in this arduous process burn cash to the tune of approximately $802 million per drug (Dickson and Gagnon, 2009). Drug discovery and development have observed an unprecedented predicament in the past ten years: few new drugs were produced and approved despite more available funding and investments. Historical experience has proven to be a significant point of initiation in the process and success of drug discovery. This is further reckoned by Sir James Black, a former Nobel laureate who stated the initiation of the drug discovery process from an old drug is the most fruitful basis for discovering a new drug. The pharmaceutical industry has reverted to the historical experience again to discover novel drug candidates from natural sources and traditional medicines (Corson and Crews, 2007) (Raju, 1999).

About the health of Chinese people amongst others who have been using traditional medicine from ancient times to maintain their health, it could be vividly considered that conventional medicine may have more indications for contemporary drug discovery process rather than new chemical drug entities. The past century's efforts of medicinal chemists have borne fruitful results in the form of accumulation of almost 170,000 drugs which is around 100 times more than the prospective drug targets, which pool around 1500 only. If we consider the point that ligand binding sites are much less varied and assorted than protein architectures, then we can be certain that existing drug candidates may have encompassed a significant number of potential drug targets (Kong and Zhang, 2009).

Nowadays discovery of drugs is grounded on lock-key drug theory which, focuses on a single potential candidate to hit one target to cure various associated diseases (Sams-Dodd, 2005). Conversely, the pathology of various ailments is multifaceted and comprises numerous aspects which make it difficult for a single drug target to defend and combat against polygenic illnesses (Zimmermann *et al.,* 2007). Additionally, inhibition of one target is a significantly less efficient non-selective approach resulting in fewer efficacies as the human body is a tremendously intricate and complex grid with a lot of redundancy in it and unexpected side effects might interrupt the balance of the grid. (Csermely *et al.,* 2005) (Reddy and Zhang, 2013). The modernization of medicine in America today has called for strengthening and development of the drug discovery process through bridging the gap bawling for mutual collaborations between industrial, academic, and philanthropic sectors. This will, in turn help in breaking the barriers to ultimate commercialization and translation by fetching superlative practices from industry to academic organizations, and this would occur not only by generating new generation translation scientists but also by producing a novel force of skilled scientists in regulatory discipline (Strovel *et al.,* 2016). For the discovery of new disease targets and development of the next generation of disease interventions, biotechnological and pharmaceutical industries have been integrating chief high-tech scientific progressions at the phenotypic, genetic, and proteomic levels for more than 50 years. But despite all these remarkable biotechnological developments, there have been very few chief progressions in the average success rates for developing novel drug candidates and identifying first-hand drug targets. However, in recent times emergence of disruptive therapeutic modalities such as tissue regeneration, cell-based therapies, and gene therapy has given illuminating hope and could prove to be the novel therapies of the future (Kelm *et al.,* 2019). The current study aimed to highlight the current practices and future of drug discovery and development. Various databases, including Scopus, Web of Science, and PubMed were utilized to search the literature (Ashiq *et al.,* 2021; Kanwal *et al.,* 2018;).

Sources of drug compounds

Natural products are still the first choice of starting material for drug discovery despite recent advances, the rise, and the integral role of combinatorial chemistry in the lead discovery process. According to current data, in the past 25 years, almost 974 new drug entities were established, out of which 63% were either natural, semi-synthetic, or natural inspired drugs. Natural products may prove to be an important tool as a source for new drug entities for advanced methods of development for certain treatments such as anti-inflammatory, antimicrobials, antihypertensive and anticancer drugs (Ashiq *et al.,* 2021; Harvey, 2008; Tanveer *et al.,* 2019).

Plant-derived bioactive materials

In the western world, before the advent of Paracelsus, most of the diseases were cured traditionally by crude drugs, which were mostly of plant origin. This has led to the formation of a genetic pool of info full of curative potential of botanical species, thus building them as an essential point of initiation for the discovery of novel drugs. The new drugs are discovered from plant secondary metabolites, which are delocalized in various anatomical parts of the plant (i.e., leaves, bark, roots, and flowers, etc.).

It requires strong botanical knowledge for the accurate identification of these bioactive plant ingredients (Balunas and Kinghorn, 2005; Latif *et al.,* 2020; Qayyum *et al.,* 2020.

Microbial species with bioactive metabolites

The main source of antimicrobial drugs are microbes which through their competition for nutrient, living space and their ability to survive the harsh conditions (i.e., prevention of proliferation of competing species) have finally passed the test of times and has proven itself to be the preferred source for the antimicrobial treatment plan. For example, *Streptomyces* species use as a source of antibiotics. However, it's crucial to mention the classical discovery of Penicillin in 1928, a Nobel antibiotic present in the bacterial culture of penicillium fungi used as a defense mechanism against another microbe (Alagarsamy, 2013; Sharma, 2020).

Marine invertebrates as a source of bioactive compounds

Currently, there is a shift towards the marine environment as a potential source of bioactive agents and drug discovery. In the 1950s, arabinose nucleosides were discovered from marine invertebrates, which demonstrated that sugar moieties other than deoxyribose and ribose could harvest novel bioactive nucleoside structures. Although 2004 marked the year of discovery of the first approved marine drug. Prialt, a ziconotide toxin extracted from cone snail, was the first FDA (Food and Drug Administration) approved marine drug used for the treatment of severe neuropathic pain. Numerous bioactive derivatives of the marine source are now going through clinical trials for the treatment of various ailments such as inflammation, pain, and cancer. Bryostatin-like agents are one such example of marine drugs under investigation as anticancer drugs (Alagarsamy, 2013; Kiuru *et al.,* 2014).

Traditional knowledge and drug discovery

The ancient ancestral knowledge is the non-documented and verbal form of treasure communicated from generation after generation and is being nurtured by ethnic societies in common and has an association with ferny floor and red lateritic soil of Purulia District of W.B and various forests. For efficient, sustainable development, good health is one of the crucial factors for the sustenance of a steady population. But extremely high cost is one of modern medicine's main attributes, which makes maintenance of global health a difficult task to accomplish. This issue could be resolved by the production of natural lead drugs discovered through the asset of traditional medicinal knowledge that would, in turn, lead to eco-friendly sustainable progression at a lower price with low side effects (Sannigrahi, 2014).

Natural lead drugs have proven to be the most fruitful basis for the progression and discovery of novel therapeutic drugs. Furthermore, due to the wider application of various molecular biological techniques, an upward trend is shown in the accessibility of new drug compounds that are expediently generated in yeast or bacteria. Also, different combinatorial methodologies focus on natural product-based scaffolds, which are in turn utilized to create screening libraries resembling drug-like compounds. This suggests that it could be expected that effective and efficient progression and application of natural products will also advance and improve the drug discovery process (Harvey, 2008).

Global traditional medicine usage and knowledge are pretty varied and diverse; however, Ayurveda, Chinese traditional medicine, and tib or Unani medicine are amongst the most popular and widely used ones. The term Ayurveda is composed of 2 Sanskrit words Ayur, meaning life and Veda means science, collectively it refers to the science of life and is dedicated towards the holistic management of disease and health. The most crucial role played by Chinese medicines and Ayurveda is the bioprospection of new drug molecules. Both holistic approaches utilized research in varied fields such as pharmacology, pharmacognosy, and chemistry (Patil *et al.,* 2014). As a result, many secondary plant metabolites have been reported which have various indications e.g. alkaloids from *Rauwolfia serpentina* have been reported for their use against hypertension, alkaloids from holorrhena for amoebiasis, curcumin as an anti-inflammatory, *Mucuna pruriens* for Parkinson's disease, piperidines for enhancing bioavailability, picrosides for hepatic protection, guggulsterons as hypolipidemic agents, baccosides for mental retention, withanolides and many other steroidal lactones and their glycosides as immunomodulators and phyllanthins as anti-viral (Patwardhan, 2005).

Tibb (also known as Unani-Tibb or Unani medication) is a widely practiced, traditional style of healthcare that draws on the basic standards of care established by Hippocrates, Galen, and Ibn Sina, the three proponents of persuasive pharmaceuticals (Avicenna). A number of axioms underpin Tibb's 'A science of pharmaceutical, the craftsmanship of care.' One is the individuality of each person, so this is a crucial part of Tibb diagnosis and treatment since it is expressed as temperament (Bhikha and Glynn, 2017). Another is the idea of Physis, or the body's natural ability to heal itself. Rather than only treating symptoms, Tibb focuses entirely on promoting inner health. The concept of body humor is the third axiom, while lifestyle Factors are the fourth. Temperament touches on humor and lifestyle Factors have a lot in common. Realistic lifestyle guidance, natural drugs, and adequate diet therapy are all part of the treatment. Tibb isn't a new or esoteric style of therapy; it has origins in traditional medicine that date back hundreds of years to ancient Greece and Persia. When the body's functions maintain a proper balance of temperaments, structure, and functions, it is said to be healthy. A temperamental imbalance, a humoral imbalance, or a tissue structure problem can all manifest as a disease. The concept of Physis is central to health, disease, and survival in Tibb. It plays a key role in the body's self-healing and self-repair processes and actively counteracting influences that cause injury and illness. It ensures that one's health is kept at its peak. Physis corrects various lifestyle factors that cause alterations in humoral balance (Bhikha and Glynn, 2017).

The importance of lifestyle factors in sustaining the ideal qualitative condition demanded by a person's overall temperament is critical to achieving optimal health. Similarly, in the management of illnesses, restoring the proper humoral balance through appropriate application of the lifestyle factors is critical, as this tackles the symptoms and the causes. Tibb therapy fully complies with physis operation. The concept of temperament, essential to diagnosis and treatment, is also adhered to in Tibb. Temperament is a combination of personality, physics, and behavioral characteristics that makes us unrivaled. The two fundamental temperaments are a composite, a primary (dominant), and a secondary one (subdominant). Humor preserves the ideal qualitative condition of a person's temper (Shirbeigi *et al.,* 2017). The right amount and quality of humor in the body and a balance between them are health results. The illness is caused by imbalances in a person's humor composition. Physical philosophy, temperament, and humor, as well as the principle of cause and effect of Ibn Sina, testify to medical science and the art of care, which offers an understanding of the etiology, the underlying pathology, and how it is digested, and ultimately which treatments are chosen. Tibb's philosophical principles are the principles of physicality, temperament. Tibb is an ideal partner for integrative medicine because the main principles of conventional therapy are not contradictory (Bhikha, 2017).

Current practices

Since time immemorial, plant therapeutic properties have been recognized. Several pathologies with plant-derived medicines have been treated. Those medicines can be used without isolation from active compounds as concentrated plant extracts. However, modern medicine calls for one or two active compounds to be isolated and purified. But there are many global health challenges in the face of diseases such as cancer, degenerative conditions, HIV/AIDS, and diabetes, which are difficult to cure in modern medicine. The "active compound" isolation has been ineffective many times**.** Drug discovery is a multidimensional question that needs to be evaluated during drug candidates' selection by several parameters, both natural and synthetic such as safety, pharmacokinetics, and efficacy (Mohs and Greig, 2017). The development of state-of-the-art technology, which improves hypotheses of drug design such as artificial intelligence, the use of organ-on-chipping, and microfluidic technologies, makes automation part of pharmaceutical discovery. As a result, the safety, pharmacokinetics, and efficacy of candidate compounds were increased rapidly in medicinal research and analysis, while new drug design and synthesis solutions based on natural compounds were developed (Moderator *et al.,* 2015). Recent analytical and computer technology developments have opened new avenues for processing complex natural products and using their structures to generate new and innovative drugs. In fact, in the era of molecular computational design, we use natural products (Grimme and Schreiner, 2018) (Ashiq and Ashiq, 2020). The detection of molecular targets of natural products and their derivatives has contributed through predictive computational software. In the future, there will be few false-positive results in drug development using quantum computing, computational software, and databases for modeling molecular interactions and foreseeing the features and parameters needed for drug development, for example, pharmacokinetic and pharmacodynamic (Thomford *et al.,* 2018).

Spaceflight offers a complex and intellectually stimulating medical environment with complex biological and developmental changes. We learned a tremendous amount in the last century about adapting people to microgravity and the strictness of interplanetary travel. But that's only the starting point of that clinical frontier, and much has to be learned as people travel to space and invest extra time in space. Earth-based medical care has long led to the selection of prophylactic and curative disease strategies. This worked well on missions near the earth when consultation can be made, communication can be relatively constant, and returns to earth are a viable option (Velasquez, 2021). However, the presence of a doctor will constantly broaden the capacities of medical care during the flight, irrespective of whether ground support is available. Ground-based medical treatment will no longer be possible when critical medical decisions are necessary as we investigate our solar system. In the meantime, a highly qualified physician with different medical and surgical skills will be needed before the permanent habitation of space stations or lunar bases with specialist doctors and modern surgical equipment. These opportunities to move are available to emergency physicians, who should perform the function of a space physician in the distinctive medical setting of space (Hinkelbein *et al.,* 2017).

The deep-sea biological system could be the source of one kind of way. It is chiefly collected as living substances that are highly valued and are therapeutically diverse. Marine therapy could be a scientific theory of improving, maintaining, and restoring well-being by anticipating and treating seafarers. The major sources of biomedical compounds are pharmaceutical, marine sponges, shellfish, green growth, Corals, Ascidians, Bryozoans, and Vertebrates. There seems to be an initial phase in the prevailing situation in India, but steps are being taken to develop a significant source of unutilized drugs. The most emphasis is given in the search for a cure for the dangerous disease. The introduction to the deep sea exposes jumpers to a series of physiological hazards. Marine remedies are the subject of clinical trials which associate long-running safety studies with a therapy protocol history. The newly discovered drug passes through a thorough testing protocol, first in the laboratory and thus through many layers of patient testing before this drug is authorized for use by the wider populace; the marine life has a vast diversity that is still untapped. Marine medicine offers new mechanisms for combating men's most vulnerable diseases, such as HIV, pathology, Alzheimer's disease, and cancer (Deshmane *et al.,* 2020).

In recent times, it has promised biotechnology as a predecessor in the path to the insurrection of human lives. Various products include novel vaccines, diagnostic devices, and new therapeutic strategies for the achievements of biotechnology at the biomedical level. However, for a drug entity to pass different development stages, it must go through significant drawbacks and pitfalls (Ravichandran and Verma, 2021). Due to the unlimited ability of the stem cells to self-renew and differentiate to generate cells and tissue from the whole of the human body, stem cell technology has revolutionized medical biotechnology over the previous decades. To rectify or replace injured cells or tissues, many attempts have been devoted to providing state-of-the-art stem cell therapies to ultimately heal serious illnesses (Lukomska *et al.,* 2019). This technological innovation guarantees the trust of serial entrepreneurs in the economic future of products and services based on stem cells. A study characterized the state-of-the-art applications of several adult stem and embryonic applications and induced pluripotent stem cells in biotechnology that represent entrepreneurial opportunities. While stem cells contribute considerably to medical research, several barriers still need to be overcome, including ethical and regulatory issues, e.g., the functional maturation of stem cell progenitors, strict guidelines on production, immune disruption, and tumorigenicity (Jossen *et al.,* 2018).

The publication has nevertheless led to the development of successful models of human-based multi-potential stem cells based health, disease-restraining mechanisms of pathology, drug detection, and toxicity testing, microfluid, "organ-in-a-dish," and 3D bioprinting medicines. It's worth noting that, as the goals of computational chemistry and bioinformatics expanded, assistance was required to reduce the number of molecules to be tested in vitro or in vivo. In recent years, there has been a surge in the number of enterprises and start-ups focusing on bioinformatics and machine learning worldwide. Furthermore, veterinary medicine is widely used in biotechnological applications today and human therapy in stem cell-based biotechnology ushers in a new era (Leelananda & Lindert, 2016). Finally, scientists with strong entrepreneurial thinking are critical for achieving economic value in medical biotechnology. As a result, we should educate the next generation of entrepreneurs and collaborate directly with institutions and financial institutions to ensure that the next generation of students is recruited and formed in a successful translation process (Duelen *et al.,* 2019).

Conclusion

Based on their history and their known vast potential for activities and structure and function variety, this study highlights the importance of plant-derived NPs as the most important source for therapeutic development. On the other hand, the new research approach is aimed at developing pharmaceuticals based on natural mixes, which are purportedly more beneficial due to potential synergistic effects, a reduction in unpleasant side effects, and an increase in the costs of single molecular medicine.

Conflict of interest

The authors declared no conflict of interest.

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