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NATURAL PRODUCTS AS SOURCES OF DRUG DISCOVERY: EXPLORATION, OPTIMISATION, AND TRANSLATION INTO CLINICAL PRACTICE

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Abstract

This paper features the significance of regular items in drug disclosure, featuring their assorted synthetic designs and natural exercises. It underscores the requirement for a multidisciplinary approach, consolidating frameworks science with innovations like genomics, transcriptomics, proteomics, metabolomics, mechanization, and computational techniques. The paper advocates for a takeoff from reductionist methodologies and an emphasis on understanding the synergistic impacts of normal item compounds. Genomics is vital in plant-based drug disclosure, empowering exact distinguishing proof of plant species and restorative impacts. Proteomics and metabolomics assist with grasping the systems of activity, target proteins, and metabolic changes. Enormous information examination upgrades drug disclosure through computational stages and AI calculations. Mechanization advances smooth out the interaction, diminishing human mistake and predisposition. Incorporating omics approaches with drug improvement works with accuracy medication and customized treatments, upgrading remedial results.

Keywords: *Natural products, Therapeutic agents, Traditional medicine, Contemporary drug discovery, Plant-based medicines*

1. INTRODUCTION

A significant global issue is the hunt for treatment options for both infectious and non-infectious diseases, such as cancer, HIV/AIDS, malaria, diabetes, hypertension, and malaria. Despite the development of treatments, these disorders still affect many different groups worldwide and have a high fatality rate [1]. To address these issues, new methods for drug development that diverge from current pharmaceutical R&D techniques are required. For the purpose of developing novel medications, research and development (R&D) on natural substances may be essential.

Plants have developed defence mechanisms against predators and environmental disturbances in every habitable habitat. Plants are able to release toxins, colours, and smells because of these compounds [2]. Modern medicine has overtaken traditional medicine in the treatment of human ailments. However, in recent decades, the use of medicinal plants for illness treatment and health promotion has increased in many countries, including wealthy ones.

Plants are the source of about 25% of all pharmaceuticals that are approved by the FDA and the European Medicines Agency (EMA). This includes well-known drugs like morphine and Paclitaxel. Tetracycline, artemisinin, doxorubicin, and cyclosporine are a few of the most well-known instances of how natural product-based drug discovery has revolutionised medicine.

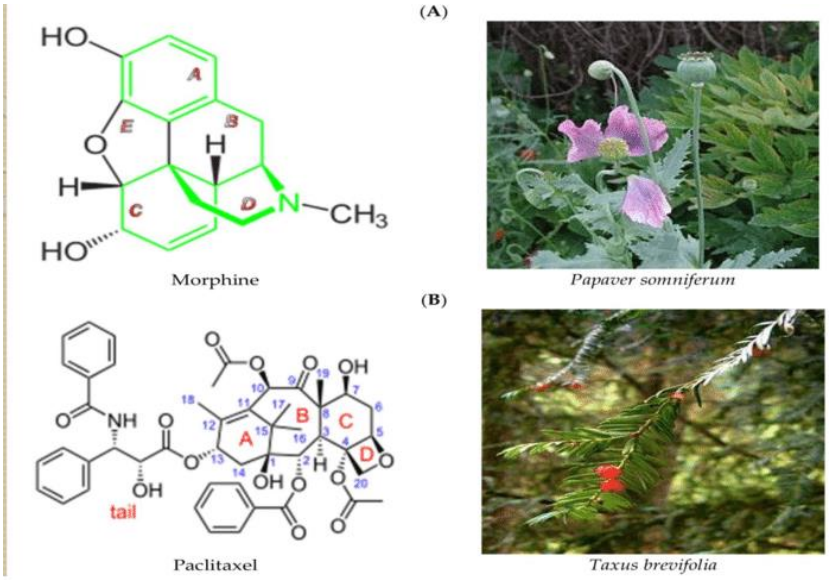

Fig. (1). Two examples of successful stories of plant natural products

1.1.NOVEL APPROACHES TO MEDICINE DEVELOPMENT USING NATURAL PRODUCTS

The creation of novel drugs begins with natural ingredients, necessitating innovative and varied methods [3]. The medicinal efficacy of natural goods is reduced when individual compounds from those items are isolated and assessed because most of the compounds show synergistic effects. New approaches must be developed for both the mixing of drugs and the assessment of their therapeutic effects. System biology approaches are utilised to provide a thorough understanding of the effects that chemicals have on organisms in order to improve medication development [4]. More effective screening methods and improved therapeutic candidates have been made possible by the application of genomes, transcriptomics, proteomics, and metabolomics in the assessment of drugs. Pharmaceutical companies are increasingly doing combination studies in an effort to create novel and improved drugs. They are eschewing the

reductionist approach of isolating and evaluating individual compounds in favour of combining them into molecular libraries.

1.2.SIGNIFICANCE OF THE STUDY

Natural products are a rich source of chemical variety and a huge resource for research into new drugs. Because of their diverse structural makeup, there is a wide range of chemical possibilities to investigate, which may contain undiscovered new compounds with medicinal potential. Through investigation of these natural products' chemical characteristics and biological functions, scientists can find promising lead compounds for future medication development. It is essential to comprehend how these substances interact with biological targets via drug-target networks in order to fully comprehend their modes of action and possible therapeutic applications. These networks act as priceless road maps that help scientists find intriguing new drug candidates and, eventually, open the door to turning natural products into treatments that are applicable to patients. Researchers can expedite the screening and optimisation process and accelerate the transition from discovery to clinical practice by forecasting the indications for these drugs. All things considered, a thorough investigation of natural goods has great potential to add new therapeutic agents to the pharmaceutical industry.

1.3.OBJECTIVES OF THE STUDY

1. To investigate and gather natural ingredients for medication development from different databases.
2. To compute and examine molecular descriptors of FDA-approved medications and natural items.
3. To examine and contrast the molecular space occupied by natural items with that of FDA-approved medications.
4. To build drug-target networks in order to comprehend how natural products interact with their targets.
5. To forecast possible uses for natural products by analysing how they interact with specific proteins.

2. LITERATURE REVIEW

Thomford et al. (2018) [5] explores the significance of natural products in the process of drug development in the 21st century. In doing so, it draws attention to the wide variety of natural products and their potential to serve as lead compounds or sources of inspiration for novel pharmaceuticals. In this study, the historical backdrop and development of drug discovery based on natural products are investigated, with a particular emphasis placed on the significance of this approach in contemporary pharmacology. In order to optimize the process, it emphasizes the use of multidisciplinary cooperation, bioinformatics, high-throughput screening, and metabolomics. This study offers a detailed overview of natural product research and the consequences that that research will have in the future.

Atanasov et al. (2021) [6] regular items are examined comparable to the course of medication improvement, with an accentuation put on the meaning of these normal items as wellsprings of bioactive particles that have a wide assortment of synthetic designs and natural action. This article underscores the huge commitments that they have made to the field of therapeutics across a great many illnesses, including neurological problems, irresistible sicknesses, and malignant growth. Normal items are featured by the creators as having the capacity to act as lead compounds, pharmacological instruments, and motivations for engineered analogs. Also,

they investigate new approaches and innovation, for example, genome mining, manufactured science, and bioinformatics, which are changing the method involved with finding and taking advantage of restorative applicants that are gotten from normal items.

Cragg and Newman (2013) [7] investigates the significance of natural products in the field of current pharmacology as a potential source of innovative therapeutic leads. The article emphasizes the different chemical structures and biological activity of natural compounds, as well as their potential as treatments across a wide range of disease areas and their substantial contribution to the pharmacopeia. Some of the methods and techniques that are used in the process of isolating, characterizing, and optimizing bioactive chemicals derived from natural products are discussed in this study. These methodology and strategies include bioassay-guided fractionation and combinatorial chemistry. The integration of genomics, metabolomics, and synthetic biology methodologies are some of the topics that are covered in this article. Additionally, it examines recent trends and future prospects in natural product-based drug development.

Bernardini et al. (2018) [8] provide a historical review of the methods to drug development that have focused on natural ingredients with the purpose of improving human health. They explore the roots of natural product research from ancient civilizations to current scientific approaches, demonstrating the interest that people have with medicinal chemicals due to the chemical variety and biological activity that they possess. In this section, they explore indigenous knowledge systems and traditional medical practices that have had a role in the discovery and consumption of natural items. Additionally, the authors investigate the influence that technical breakthroughs and scientific discoveries have had on natural product research, highlighting the continuous significance of these developments in the process of drug discovery in the process.

Kibble, M., et.al.,(2015) [9] it is generally perceived that a frameworks level polypharmacology approach is frequently expected for drug discovery to handle issues such the developing protection from the ineffectualness of single-designated compounds. To an ever increasing extent, scientists are going to arrange pharmacology strategies to find new treatment open doors and track down new purposes for existing drugs. Natural item research has been delayed to receive the rewards of these innovative developments. To work on the druggable space of proteins associated with a scope of complicated sicknesses, we contend that an organization pharmacology approach would successfully plan the objective space of natural products. We audit the vital ideas of organization pharmacology and the latest trial computational techniques that have been effectively applied to the investigation of natural products. Deliberate forecast of compelling treatment blends and objective clarification of activity instruments are two instances of the techniques that fall under this class. Our emphasis is on malignant growth medicines that utilize practical phenotypic evaluations in vitro and in vivo. Estimations, for example, all inclusive transcriptome reaction profiles empower worldwide displaying of multi-target action at the phase of natural pathways and collaboration organizations. Moreover, we give infection explicit data sets, instruments, and contextual investigations. Natural item research in the future could profit from these current and future assets. At long last, we give our singular perspectives on the ongoing restrictions, potential future ways, and extraordinary inquiries in this charming region.

Najmi, A., et.al., (2022) [10] significant source of novel lead chemicals for drug development research is found in natural products. Many pharmaceuticals that are currently in use were developed from natural sources; plants are particularly significant in this regard. Drug discovery for natural products has received little attention from pharmaceutical corporations in the last few decades, primarily because of its inherent complexity. The obstacles have recently been considerably addressed by technical developments, which has led to a resurgence of scientific interest in natural source drug discovery. Through the application of contemporary drug-development concepts of plant-based natural products, this review offers a thorough overview of the numerous methodologies employed in the selection, authentication, extraction/isolation, biological screening, and analogue creation. The bioactivity-guided fractionation technique, related difficulties, and significant developments are the main topics of discussion. Additionally provided are a synopsis of the notable natural medications created in the recent few decades as well as a brief history of the evolution of drug discovery from natural products. According to the researcher's opinions, the effective development of natural products requires an integrated interdisciplinary approach that makes use of technical advancements. These include the use of effective selection methods, carefully thought out extraction and isolation processes, sophisticated structural elucidation tools, and high-throughput bioassays to determine whether phyto-compounds are patentable and pharmacologically viable. To improve natural product drug discovery research, a variety of contemporary techniques are being applied, such as database mining, virtual screening, natural product libraries, and molecular modelling. Natural products will undoubtedly play a significant role in the future development of new therapeutic drugs, as demonstrated by the renewed scientific interest and recent research trends in this area. It is also anticipated that the successful implementation of novel approaches will enhance the drug discovery campaign.

2.1.Research gap

Despite the way that the review gave a complete examination of natural products as potential hotspots for drug discovery, there are huge exploration holes that poor person been tended to. The coordination of information from numerous omics, including genomes, transcriptomics, proteomics, and metabolomics, can possibly give a more far reaching comprehension of the organic exercises of natural products. What's more, albeit an expectation model for sickness signs that depends on drug-target communications has been introduced, there is an absence of observational affirmation through research directed in vitro and in vivo. Moreover, the potential synergistic collaborations that might happen between natural products and drugs that are now being used, as well as the contemplations of environmental manageability in the usage of natural products, are regions that require further exploration. Should these lacks be tended to, the information premise that upholds the therapeutic pertinence of natural products would be fortified, and the most common way of making an interpretation of natural products into clinical practice would be worked with.

3. RESEARCH METHODOLOGY

3.1. Assortment of Natural Products and Endorsed Drugs

The natural products were obtained from numerous data sets, including Reaxys, INPD, TIMD, and our own IHDD, which represents Indian Wellbeing Information Data set. In Table 1 you can see the absolute number of compounds in every one of the data sets along with the all out number of compounds with copy structures. Discovery Studio designed and assembled the

three-layered developments. While managing certifiable articles, the outright setup is utilized. We distinguish two outright designs and dole out a particular number to every one for structures that are not completely clear, like R/S or Z/E. The greater part was kept and the more modest part was taken out when a solitary construction was parted down the middle (like salts or adducts). The InChIKey that Open Babel provided was utilized as a manual for erase the duplication. This guarantees that there is a particular stereochemistry for each particle in UNPD. Utilizing the MMFF94 force field, we had the option to diminish the impacts of each and every compound design. There were inquiries over the sythesis of endorsed prescriptions, as per a download from DrugBank.

Table 1: The number of chemicals and structural duplicates found in each database.

Database	IHDD	INPD	TIMD	Reaxys
Total Compound	30574	57014	23014	174584
Used in UNPD	29568	47125	7500	114587
Duplicates	780	15036	15469	54857

3.2. Statistics and Calculation of Molecular Characteristics of NPs and Medications

The molecular descriptors of the drugs and NPs were calculated in Discovery Studio with the default settings, as shown in Figure 1 and Table 2. Three hundred substructure descriptors and a substructure-related molecule descriptor were calculated using a free tool named PaDEL Descriptor.

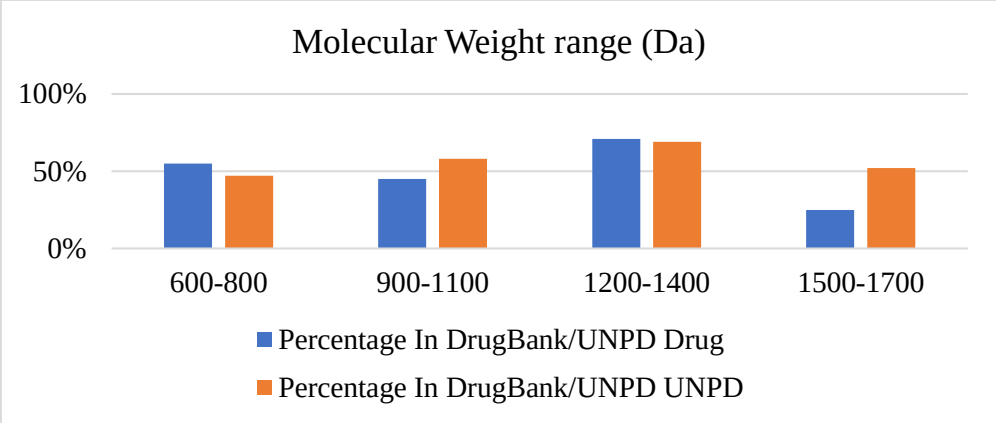

Fig (2) (a): Four molecular characteristics of natural goods and authorised pharmaceuticals and their distribution

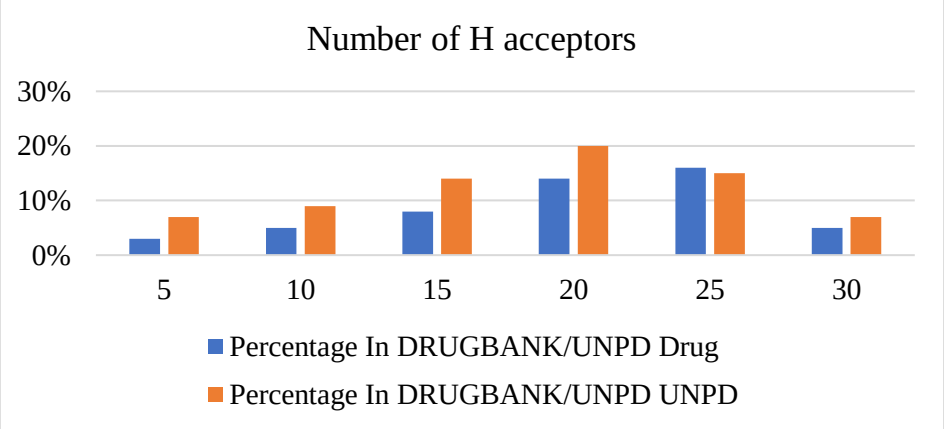

Fig (2) (b): Four molecular characteristics of natural goods and authorised pharmaceuticals and their distribution

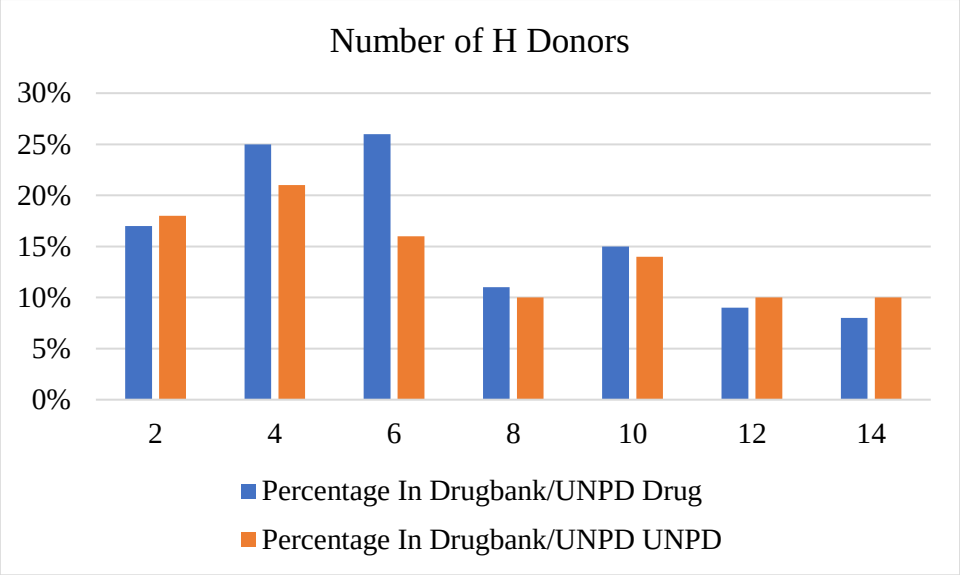

Fig (2) (c): Four molecular characteristics of natural goods and authorised pharmaceuticals and their distribution

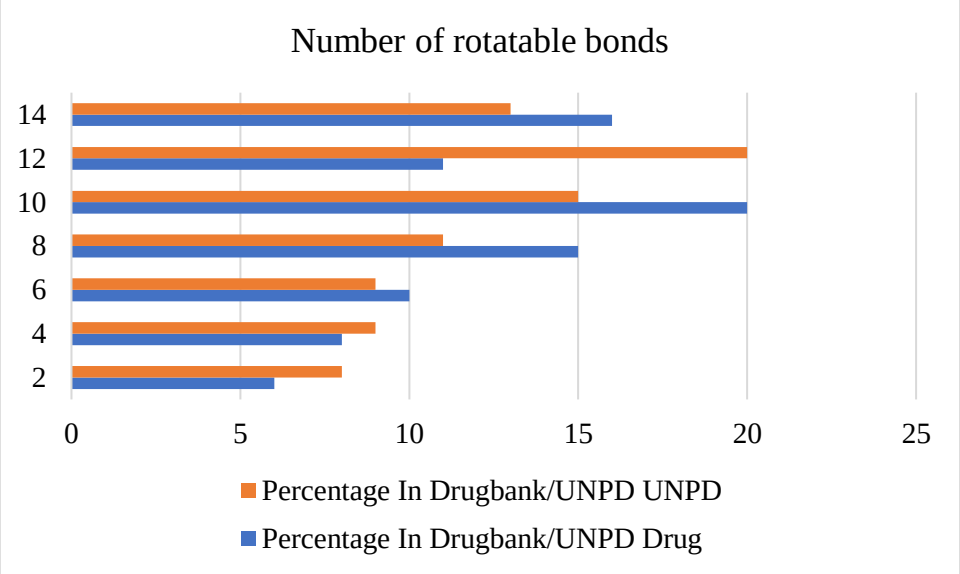

Fig (2) (d): Four molecular characteristics of natural goods and authorised pharmaceuticals and their distribution

Table 2. Molecular descriptions of natural products and statistics on drugs approved by the Food and Drug Administration are both housed in DrugBank.

Descriptors		**Natural Products in UNPD**				**Approved drugs**		
	Mean	**Median**	**Min**	**Max**	**Mean**	**Median**	**Min**	**Max**
AlogP	2.655 ± 2.351	2.612	-30.006	52.415	1.765 ± 2.714	1.154	-12.141	13.142
Molecular Weight	3.125±161.5	301.4	15.0	2174.6	2610±195.1	212.1331	5.2	1529.1

Num Rotatable Bonds	5.6±5.6	4	0	130	4.5±3.1	3	0	35
Num Rings	2.5±1.3	2	0	25	1.5±1.5	2	0	5
Num Aromatic Rings	1.6±2.1	0	0	15	1.2±1.1	1	0	7
Num H Acceptors	6.4±5.4	5	0	101	4.2±3.1	3	0	45
Num H Donors	2.2±4.1	1	0	55	2.2±1.6	3	0	21

3.3. Chemical Space Analysis

Involving the library examination module in Discovery Studio, we ran head part examination (PCA) in the wake of posting the information boundaries as a whole. Utilizing head part examination (PCA), a symmetrical direct change technique, our exploration information was changed into a three-layered coordinate framework. Boosted information fluctuation on the main direction is what we mean when we discuss the primary head part. We boosted the excess minor departure from the subsequent direction, and progressed forward with that way. The chief part examination (PCA) model was assembled utilizing eight descriptors: AlogP, Atomic Weight, Num_H Contributors, Num_H Acceptors, Num_Rotatable Bonds, Num_Rings, Num_AromaticRings, and Sub-atomic FractionalPolar Surface Region. These descriptors were not pre-scaled. contrasts in the third PC, second PC, and first PC for drugs and UNPD.

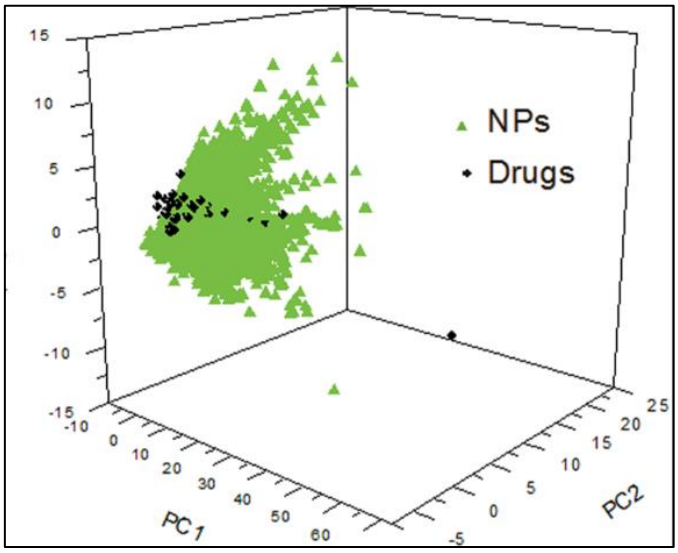

Fig.(3): Chemical space distribution of UNPD and FDA-approved medication natural product components as determined by principal component analysis

The green triangles and dark specks address natural products and FDA-endorsed drugs, individually.

3.4. Constructing of DTNe

We got the trial restricting information for natural products from BindingDB on October 21, 2011. Natural synthetic compounds in BindingDB were distinguished by contrasting sub-

atomic designs utilizing InChIKey. We saved the limiting information for focuses with their own exceptional UniProt passages. Cytoscape (DTNe) was utilized to associate NPs and trial focuses to develop the drug-target network in light of exploratory information. The organization properties and hub centralities were all determined by CentiBin and the module for the organization [15-20].

3.5. Constructing of DTNd

The authorized meds remembered for DrugBank and their objective proteins were alluded to as "focuses" in the data set. With admittance to 4152 objective proteins in the RCSB Protein Information Bank, we had the option to assess potential lead compounds utilizing precious stone or NMR structures. The protein-ligand complex designs of approved drugs' objective proteins were recovered from DrugBank. Hydrogen iotas were fill in for heteroatoms utilizing Discovery Studio. To assess the NPs' partiality for their objectives, the principal ligands inside the complicated designs were utilized as reference atoms. The 40 × 40 × 40 Å 3D shape, with 0.375 Å between the framework focuses, and fixating on the first ligand's consumed space, was utilized to decide the limiting site of each target protein. To deal with docking in DOVIS 2.0, autodock4.01. Produce a drug-target organization (DTNd) utilizing docking information was indistinguishable from create a DTNe.

4. RESULTS AND DISCUSSION

4.1. Data Analysis of Natural Product Molecular Characteristics and Comparison with Pharmaceuticals Regulated by the Food and Drug Administration

Fundamental atomic elements of drugs endorsed by the FDA found in DrugBank and naturally happening substances in UNPD. In contrast with drugs endorsed by the Food and Drug Organization, the factual means and standard deviations of natural items were normally bigger. These perplexing and various compound designs of natural substances could give upgraded polypharmacology because of their associations with a few objective proteins.

It was normal practice to utilize Lipinski's "rule of five," got from measurements on oral drug, during the primary screening process. While looking through monstrous datasets for synthetic substances with medicinal properties, Lipinski's "rule of five" can be useful, but wemi-observational guidelines aren't precise all the time. The drug-like properties are involved four primary, separately restricted perspectives: a sub-atomic load under 500 Da, various hydrogen security benefactors (HBD) under 5, a segment coefficient AlogP under five, and various hydrogen security acceptors (HBA) under ten. In a new article, Leeson featured how Lipinski's standard of five could deceive drug discovery since a few fruitful drugs didn't meet each of the four cut-off boundaries. We took a gander at the satisfied circumstances for all natural products in UNPD, and just 10,2605 (or 52.0% of the aggregate) of the 72,301 things were natural. In any case, 141628 (71.8%) of the natural things met each of the three cut-off prerequisites. Meds represent 1,380 (1065, or 77.17 percent) of the aggregate; utilize the "rule of five." Amount of atoms fulfilling each of the four measures or three of them, with marginally unique edge values. Reason can't help suspecting that more hydrogen bond givers and acceptors would be available at a bigger sub-atomic weight. Moreover, there is little uncertainty that AlogP's relationship to these traits is indistinguishable [21-28].

Table 3. Reports on natural products that meet the "rule of five" standards in UNPD and on tiny pharmaceuticals that have been approved in DrugBank.

Rule of Five	UNPD (Total 197845)	Drugbank (Total 1358)
All satisfied	102458	1025
Except mw	112548	1074
Except acceptors	102548	1075
Except Donor	106325	1005
Except AlogP	120054	1106

4.2. Drug-like Space and Lead Compounds Discovery from Natural Products

It was essential to have the commonly held belief in drug-like chemical space in order to conduct drug discovery. The neighbourhood activity of natural things was found to be similar to that of pharmaceuticals when Rosen and colleagues investigated the chemical space occupancy of natural substances. The chemical space allows us to compare potential lead compounds to FDA-approved drugs, allowing us to filter through enormous chemical libraries. Fewer chiral centres and more aromatic or heterocyclic centres were seen in medications, which is consistent with the results of a recent study. The median F-Chirality value in DrugBank is 0.45, the mean value in Natural Goods is 0.44, and the standard deviation is 0.38. F-Chirality is defined as the fraction of carbon atoms that are chiral relative to the total number of carbon atoms. It proves that medications had more chiral centres than natural commodities. However, compared to pharmaceuticals, natural commodities have a larger chiral carbon count due to the higher overall carbon content of these goods. There were less other features compared to natural products overall. Two groups of molecules were better understood by creating a chemical space representation of them using principal component analysis. It was expected that NPs will possess a wide variety of features due to their dispersed nature in chemical space. There was a lot of overlap in the chemical space, suggesting that natural products could be a great resource for medication development.

4.3. How Natural Products Act on Living Things

The vast array of biological tasks that natural products are capable of performing is a direct result of their ability to interact with different cellular targets. There are already more than 17,000 entries of these types of interactions registered in BindingDB and ChEMBL. We constructed a drug-target network (DTNe) by linking the natural compounds with their experimental targets after extracting the interaction data (Tables S1).

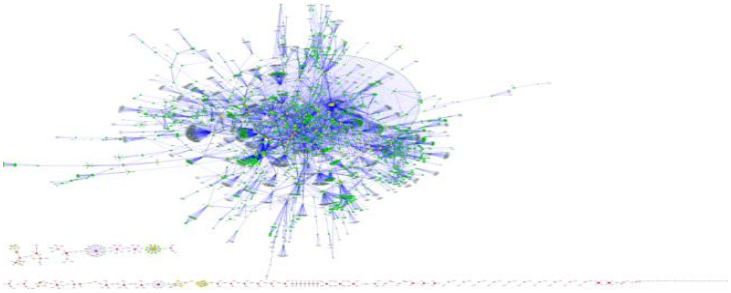

Fig. (4): DTNe, or drug-target network of natural products, is a kind of drug discovery tool.

The size of every hub is straightforwardly corresponding to its certification. In this organization, every hub is shaded by the briefest way associating them. Proteins that are expected to be designated and little particles (like drugs or natural substances) are addressed by triangles and circles, separately.

The two essential measures used to decide a hub's significance in an organization were its certificate and its betweenness centrality. A hub's certification in an undirected chart is equivalent to the quantity of neighbors it has. The significance of hubs to the organization's information move was reflected by their betweenness. The hubs that had the best level of neighborhood network (as estimated by betweenness) and the most extensive level of worldwide centrality (as estimated by degree centrality) were called center points and bottlenecks, separately. The effect of these hubs on the organization overall would be significant [29-43].

The DTNe organization, like most of natural organizations, showed a regular sans scale circulation with a degree conveyance of 180.77*×Λ(−1.125) and a connection coefficient of 0.84. This would be exceptionally useful for both the transmission of data and the strength of the organization. A 2.66 normal and a couple of exploratory objects were normal among natural things. A few natural compounds, in any case, had an excessively large number of targets; models are UNPD49205 (82 targets) and UNPD68000 (298 targets). A natural compound got from the Streptomyces bacterium known as UNPD68000 (staurosporine, STS) was disengaged. The vitally natural job of STS was to connect to the ATP-restricting site of protein kinases with extraordinary partiality and specifically repress them. Midostaurin, a novel and exceptionally productive kinase inhibitor, was created from staurosporine. The anticancer impacts of a few staurosporine cognates are being concentrated on in clinical preliminaries right now.

A flavonoid known as quercetin (UNPD49205) was available in various plant species. Its cell reinforcement activity was comparable to that of various other phenolic heterocyclic compounds. Numerous illnesses, including malignant growth and infections, have answered decidedly to quercetin's treatment. Moreover, quercetin has been exhibited in numerous cell and creature models to hinder the development of disease cells at various stages straightforwardly.

Both STS and quercetin showed significant betweenness centralities and had huge degrees. Notwithstanding, there were a couple of natural synthetics that showed low degree however huge betweenness centrality in DTNe. Various plants contain the well known isoflavone genistein, or UNPD152676. A portion of genistein's many realized organic capabilities incorporate diminishing free extreme harm and impeding the activity of the epidermal development factor receptor. It was likewise recommended that inhibitting the development of malignant growth cells could be utilized.

Natural products can be utilized as a compound library for drug discovery because of their different organic exercises. In any case, there wasn't sufficient data about how natural compounds communicate with cell targets. On account of the persistent enhancements in PC innovation, we can produce an adequate number of information through high throughput virtual screening. The atomic docking method created via AutoDock4 was hence utilized to reenact the connections that exist between organic targets and natural products.

Fig. (5): A network that links computational targets with natural product drugs.

Natural product targeting in DTNd averaged 2.14 target proteins, with 25 hits (natural product targeting) per target protein. The value of DTNe was 2.66 and 5.35 at the same time. Because of this, it seems that most natural products have not been tested for their biological function in labs. The construction of DTNd involved fifteen subgraphs. There were 28,010 natural compounds and 228 target proteins in the massive component, which made up 98.6% of the nodes in the subnetwork. Still, there were 110 subgraphs that comprised DTNe, with the huge component accounting for 90.1% of the total nodes. This is why there is a severe lack of method in the present literature regarding the biological roles of natural products; perhaps, large-scale molecular docking could fill this gap.

Table 4: General characteristics of three drug-target networks.

DTN	No. of compounds	No. of targets	<node degree>	<shortest path>	Network Density
DTNd	2845	240	3.85	4.31	0.0012
DTNe	2891	1548	3.50	5.41	0.0007
DTN*	1249	1354	3.60	7.15	0.0015

Drug Target network of pharmacological targets in Drugbank for FDA-approved medications. a list of natural products with their CAS numbers, degrees, betweenness centrality scores, chemical names, and unique identifiers (UNPD IDs) included. These numbers show how important and connected each molecule is in a drug-target network. Particularly, substances such as Vatamine (UNPD141622) and Ormojine (UNPD43323) have strong betweenness and degree centrality, indicating a major role in interactions with several target proteins. On the other hand, substances such as Seldomycin 5 (UNPD2675) demonstrate reduced network connection. In general, this table provides information about the properties of the network and possible pharmacological significance of these natural chemicals.

Table 5. Most potential natural products for lead discovery.

UNPD ID	Chemical name	CAS	Degree	Betweenness
UNPD43323	Ormojine	14710-60-8	85	0.075

UNPD194973	Ormosinin	Not Available	60	0.040
UNPD107682	Vatamidine	125441-47-3	48	0.020
UNPD141622	Vatamine	129700-80-5	80	0.021
UNPD61603	Strychnohexamine	448759-24-8	70	0.026
UNPD38223	Caledonine	235698-25-6	84	0.010
UNPD21224	Lycopodium Base B	54865-30-4	60	0.015
UNPD5255	Vatine	129648-50-0	28	0.019
UNPD41999	Lycopodium Base A	540321-30-8	31	0.014
UNPD2675	Seldomycin 5	569748-26-4	26	0.005

4.4. Predicted Diseases for Natural Products

For thousands of years, natural products have been employed as medical treatments. But it was rarely possible to determine the chemical process with clarity. Here, we used DTNd to forecast the possible indications for natural goods. Natural products, particularly high-degree molecules, usually interact with several target proteins, which are implicated in a variety of disorders. Following the extraction of target-related disorders from the Therapeutic Targets Database, we built the docking score-weighted prediction model shown in the following figure to forecast the likelihood that a natural product will be used to cure specific ailments [44-56].

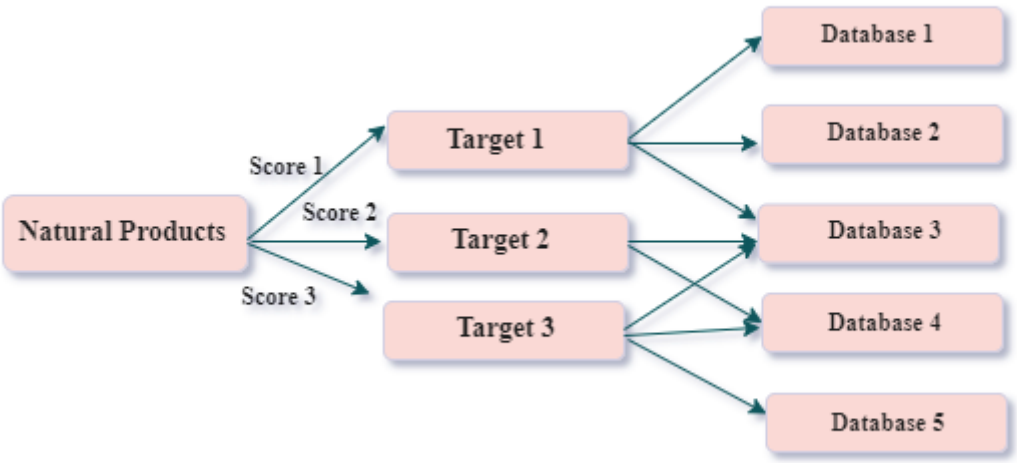

Fig. (6): Prediction model of indications for natural products.

Pridiction coefficient = $\sum \iota \in T \text{Score}\iota$

Table 6. Predicted indications for natural products.

Natural Products	Prediction coefficient	Indications
UNPD197980	58.15	Bacterial Infections
UNPD43365	55.36	Prostate cancer
UNPD43365	50.45	Asthma

UNPD43365	50.00	Cancer, unspecific
UNPD107682	48.45	Bacterial Infections
UNPD141622	50.14	Prostate cancer
UNPD141622	51.51	Asthma
UNPD141622	54.20	Cancer, unspecific

5. CONCLUSION

We investigated the potential of natural products as sources for drug discovery, optimisation, and clinical use. Our study covered a wide range of natural product applications. We painstakingly collected a wide range of natural products from different databases and carried out comprehensive investigations, such as molecular descriptor computation, chemical space exploration, and drug-target network design. These efforts have provided us with important new insights into the wide range of biological activity and molecular diversity present in natural products. Our research demonstrated how natural materials differ from FDA-approved medications in their molecular makeup, indicating the possibility of polypharmacology and a wide range of therapeutic uses. Even while they didn't always fit Lipinski's "rule of five," a sizable percentage of natural compounds showed characteristics similar to those of drugs, highlighting their potential as therapeutic possibilities. Investigating the chemical space produced interesting intersections between FDA-approved medications and natural items, suggesting that natural products could be sources of lead compound development. Furthermore, by illuminating the complex relationships between natural products and their computational or experimental targets, our research of drug-target networks provided insights into the range of biological activities and potential therapeutic applications of these compounds. Our research demonstrated the value of computational methods, including molecular docking, in enhancing experimental data and enabling methodical investigation of the biological properties of natural products. We have contributed significantly to the understanding of the therapeutic use of natural products by finding high-degree chemicals and forecasting their possible applications. Our thorough investigation reveals the unexplored potential of natural products in drug discovery, providing a viable path for the investigation, improvement, and application of these substances in therapeutic settings. By utilising nature's pharmacopoeia, we can address unmet medical needs and open up new treatment modalities as we continue to leverage advances in computational technology and enhance our understanding of the chemistry and biology of natural products.

5.1. FUTURE SCOPE

The field of natural product-based medication discovery has a wealth of untapped potential for research and development. Prospective investigations could explore the extensive molecular area occupied by natural compounds in greater detail. By means of thorough examination and investigation, scientists can find new substances with distinct chemical characteristics that could be excellent candidates for pharmaceutical development. Using computational approaches in conjunction with experimental validation is a critical step towards improving the efficacy and precision of drug development initiatives. The identification and optimisation of medications generated from natural products can be accelerated by researchers by utilising computational methods in conjunction with empirical data. Furthermore, there is a lot of

promise in studying the interactions between several targets and synergistic effects of natural compounds. Gaining insight into how these substances interact with various biological targets can help design polypharmacological medicines that more effectively treat complex disorders. Furthermore, there is potential for improving the bioavailability and therapeutic efficacy of medications produced from natural products in clinical settings through the investigation of novel drug delivery systems and formulation techniques. Researchers can overcome difficulties related to formulation and administration by utilising developments in drug delivery technology, which will eventually lead to the development of natural product-based medicines in clinical practice. To fully realise the therapeutic potential of these molecules, a multifaceted strategy that incorporates both scientific innovation and technology advancement will be key components of the future of natural product-based drug discovery.

ABBREVIATIONS

R&D = Research and Development
EMA = European Medicines Agency
CETSA = Cellular Thermal Shift Assay
TPP = Thermal Proteome Profiling

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