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Drug Design and Development

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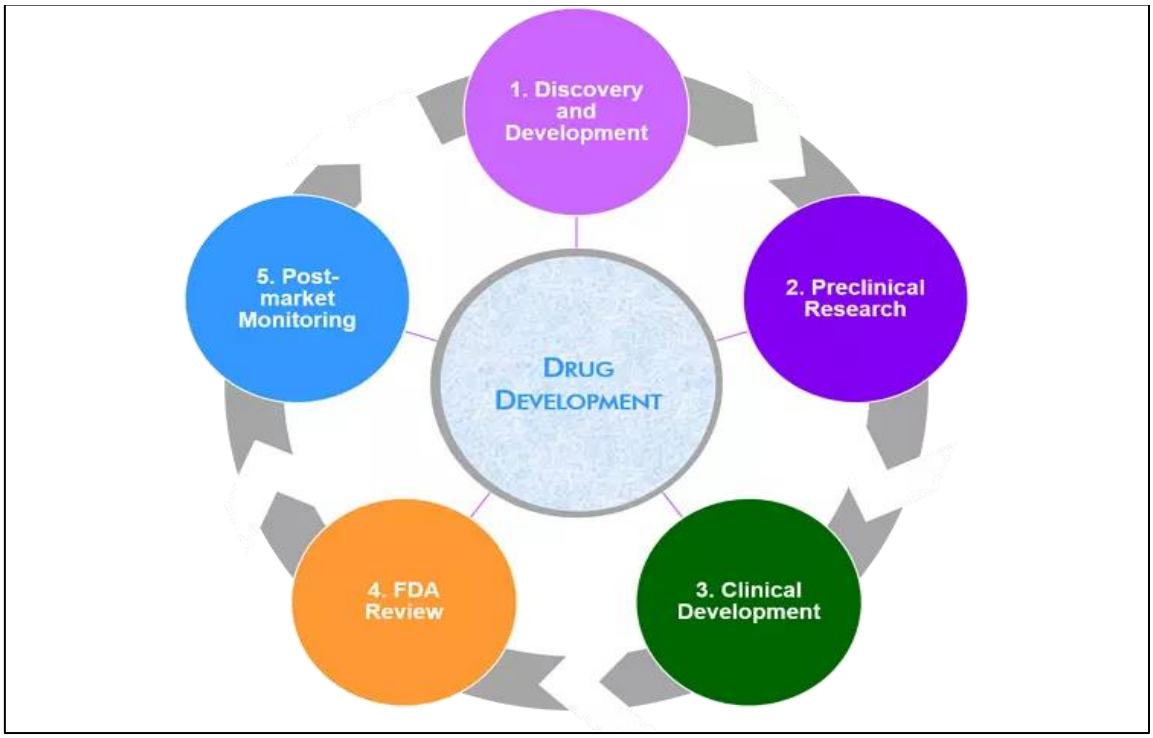
Abstract:
A common name for drug design is rational drug design or just rational design. The study of molecule shape is defined as figuring out how molecules adhere to cell receptors or connect to other molecules to trigger a certain reaction .It is supported by Instead of blindly evaluating hundreds of molecules to discover if one or more of them bind cellular or molecular targets, one might use the shape or architecture of the molecules themselves. The drug is an organic substance. When a biomolecule attaches to the target site, it can either inhibit or increase the activity of the biomolecule, producing a therapeutic effect. Development of drug is an very complex process which can take up to around 5-10 years and cost $1.8 billion. A novel development's inspiration might come from a number of places, such as market demands at the time, newly emerging diseases, academic and clinical research, the private sector, etc.[1-2]

Keywords: Drug design, Drug Discovery, Design techniques, Drug development , Clinical research (Trials)

Introduction:
The creation of new medications is an expensive, risky, and challenging process. Its success is heavily reliant on the close coordination and interaction between several divisions within the drug development organization, external investigators and service providers, in continual communication with regulatory authorities, patients, academic experts, organizations for patients and practitioners. Drug development is by far the most complex of the several stages of the drug life cycle, the most important factor in determining a drug's initial and ongoing success on the market. The study's initial results would be the identification and examination of certain receptors (targets) in the area of expertise. The detected targets must then be modified to change their engaging in protein receptor or target action. Finally,
A drug scientist finds the healing substance in order to interact with the receptor, the medicinal substance might either artificial or naturally occurring. Drug development, among the several stages of the drug life cycle, is by far the most important aspect for the beginning and ongoing success of a drug development. .Once a compound that fulfills all of these requirements has been identified, it will begin the process of drug development.[3-5]

Objectives-[6]
Identify the stage-specific success rates for experimental drugs.
- Describe pre-clinical research.
- Describe Phase I, Phase II, and Phase III investigations for Investigational new Drug Applications.
- Clarify the new Drug Application

- Describe investigations in Phase IV.



Period in drug discovery and development process-[7-11]

According to estimates, the entire drug research and development process takes between 5 and 10 years to complete, costs $1.8 billion, and takes between 5 and 10 years to effectively bring a medicine to market. The several stages/phases in the discovery and development of drugs are: [7-11]

Period of Drug Discovery [12–18] Discovery and development include:

- Target identification
- ♦ Target validation
- Lead identification
- Lead optimization
- Product characterization and Formulation and development.
- Investigational new Drug
- New Drug Application
- Clinical trials Approval

Modern Technologies of Interest for the Process of Drug Development.

Education Activities carried out to promote DRUG DISCOVERY AND DEVELOPMENT.

Drug discovery-

- Researchers now discover the new drug through:
- Research into a disease process that inspires scientists to develop a novel treatment to halt or reverse the disease [32-33]
- Numerous molecular compound assays to identify potential therapeutic effects against a wide range of disorders

- Existing therapies with unexpected side effects [34-39].
- New technologies, such as those that allow medicinal goods to be targeted to particular areas inside the body or to modify genetic material [40-42].
- Thousands of chemicals may be possible candidates for development as a medicinal therapy at this point. However, after first testing, only a limited number of compounds appear promising and warrant additional investigation [43-45].

Drug Development-

- Once a promising molecule has been chosen for development, researchers do tests to learn more about [46-50]:
- How it is Absorption, metabolized, distributed, and eliminated
- Its possible advantages and action methods
- The most effective method of delivery and dose
- Adverse reactions, also known as toxicity
- How it differs in its effects on various racial, ethnic, and gender groupings.
- The way it works with other medications and therapies
- Its efficacy in comparison to drugs of a comparable kind.

Methods/technique of drug design-:

1) Docking-[96]

A computer technique called molecular docking can be used to determine the architecture of compounds made up of two or more different molecules. In order to predict how a ligand will interact with a target protein, docking is frequently utilized in relation to activity and affinity. Docking is essential to the rational design of pharmaceuticals. Thinking on the biological and Considering the pharmacological significance of docking investigations, substantial work has been done to enhance the docking prediction methods. Docking is a mathematical method that foresees one's preferred orientation. Molecule in relation to another (perhaps a medication with a ligand, or a target protein with a rocesses a binding site) when they are connected to form a stable compound. The strength of the scoring functions (binding energy) may be calculated by a joining or binding .

Docking types:

Rigid docking-

In the event that the compounds are rigid, we are looking to rearrange one of the chemicals that produce the best match to the other compounds in three-dimensional space specifications for a scoring system. With or without the ligand, the conformation can be produced by binding activity for receptors.

Flexible docking

In addition to transformation, we assess cellular adaptability to find confirmations for the molecules of the receptor and ligand when they are combined.

Applications:

- Lead optimization
- Hit identifications
- Drug DNA interactions

Pharmacophore-[95-99]

- Paul Ehrlich first proposed the idea of a pharmacophore in the early 1900s. In his 1960 book Chemobiodynamics and Drug Design, Schueler first used the word "pharmacophore," which he described as "a molecular framework that carries (phoros) the essential features responsible for a drug's (pharmacon) biological activity."
- In those years, a pharmacophore was thought to be a molecule's chemical or functional groups that are in charge of its biological activity.
- The International Union of Pure and Applied Chemistry (IUPAC) defined pharmacophore as the total of the steric and electronic qualities necessary for a molecule to interact with a target and produce biological activity in 1997.
- A pharmacophore is an abstract symbol that does not represent a specific molecule or combination of chemical compounds.
- Each atom or group in a molecule that exhibits molecular recognition-related characteristics can be changed into a pharmacophore pattern. The patterns of molecular pharmacophores might be hydrogen bond acceptors (HBA), donors of hydrogen bonds (HBD), or positive.
- Aromatic rings, hydrophobic characteristics, negative features, and their combinations.
- A 3D (three-dimensional) arrangement of several patterns makes up a pharmacophore model.
- Pattern with the dimensions. A typical sphere with a radius that represents each design is defines the tolerance for variation from the precise location. There are also plenty additional showing the way. These designs may be shown individually or in combination.
- Pharmacophore modeling strategies
- There are two main methods of pharmacophore modeling that are applied in the process of finding new drugs: Structure-based and ligand-based pharmacophore modeling are two options.
- A collection of active ligands is used to design new ligands in the ligand-based pharmacophore modeling technique. If the target structure is not available, this strategy is used. Similar to this, when the target protein's structure is known, the structure-based pharmacophore method is used.

Drug Design Based on Ligands

- The initial active ligands in the ligand-based pharmacophore modeling are found through database searches or literature searches. A training set and a test set are created from the data set.
- After that, the training set ligands' feature analysis is carried out. The alignment of the active ligands allows for the detection of the shared characteristics.
- The creation of pharmacophore models and ranking of the models that are produced come next.
- The optimal pharmacophore model is then chosen in accordance with the findings of the pharmacophore model validation.

Modeling of Pharmacophores Based on Structure

The initial stage in structure-based pharmacophore modeling is choosing and preparing the target protein structure. Prediction of the binding location is the next step. The binding site amino acids' complementary chemical characteristics and their structural arrangements are then determined by carefully examining it. Then, using the modified tools, the pharmacophore characteristics should be tuned are produced in the programs used.

The activity-causing pharmacophore properties that are most important are then chosen. Snooker, MOE, LigandScout, and Pocket v2 are some of the popular programs for
Modeling of pharmacophores based on structure. Likewise, a variety of software and servers used for modeling pharmacophores.

Applications:

1) Pharmacophore modeling is employed in virtual screening, fishing drug targets, ligand profiling, docking, and ADMET prediction.
2) New perspectives are also expected for various applications of …….of the concept. In this way, besides the applications explained here, it may have applications in polypharmacology, drug repurposing and side effect prediction

2) Quantitative Structure Activity Relationships (QSAR):

QSAR is a mathematical or statistical approach to defining the relationship between a molecular system's biological activity (based on experimental data) and its geometrical, physical, electrical, and chemical characteristics.
Activity is equal to function (property 1, property 2, etc.). Activities equal functions (xi)
Descriptor: xi
Geometry,sterics, or sterics, etc. Design of analogous drugs
The study of structurally distinct, pharmacologically active compounds is where analogue design is most successful since these molecules' biological activity is influenced by both the nature and the specifics of their chemical structure.
Therefore, a small change to the molecule may have a significant impact on how the pharmacological response behaves (it may intensify, reduce, vanish entirely, or change completely).
It is common practice to classify lead substances as endogenous participants (hormones, neurotransmitters and second messengers).

Applications:

1. Information from the intercept values
2. Information in drug research
3. Enzyme inhibition
4. Information on receptor site
5. Bioisosterism

4) Chemistry combinatorial

Chemical synthesis techniques known as combinatorial chemistry enable the production of numerous compounds—tens of thousands or even millions—in a single procedure.
These compound libraries can be created using computer-generated chemical structures, sets of individual compounds, or mixes.
It is the technique by which large number of different but structurally similar molecule core produced rapidly and submitted for pharmacological assay.
The technique used same reaction condition within same reaction vessel to produce a large range of analogue.

Applications:-

1) Synthesis of Peptoids
2) Combinatorial lead optimization of a neuropeptide-ff antagonist.
3) Generation of a benzodiazepine library.
4) Combinatorial lead optimization of histamine H3 receptor antagonist.
5) Combinatorial lead optimization of dihydrofolate reductase inhibitors .

Preclinical trail-[51-65]

Before testing a medicine on humans, researchers must determine if it has the potential to cause substantial damage. Preclinical research is carried out on animal models in a laboratory setting [51].

There are two categories of preclinical research:

- In Vitro: These investigations are carried out outside of animals in a controlled laboratory setting [52-55].
- In Vivo: These investigations are carried out within the animals [56-57].

Preclinical investigations are often small in size. These studies, however, must offer thorough information on dose and toxicity levels [58]. Following preclinical testing, researchers evaluate their findings to determine whether the medicine may be tried in humans [59-60].

Among the experiments carried out throughout these research are [61-65]: Toxicity studies with a single dosage

Dose-repetition studies

Safety pharmacology research Genotoxicity research Carcinogenicity research.

Clinical research-[66-76]

While preclinical research provides answers to fundamental issues regarding a medicine's safety, it is not a replacement for studies of how the drug will interact with the human body [66].

The term "clinical research" refers to human investigations or trials. As the developers construct the clinical trial, they will assess what they aim to achieve for each of the Clinical Research Phases and start the Investigational New Drug Process (IND), which must be completed before clinical research can commence [67-70].

Investigation of new drug application-

INDA is used after successful preclinical studies, and if the INDA filing is accepted, the product is moved to clinical research studies (Phase I - Phase IV studies) [71].

Drug design clinical trail-

Clinical trials are created by researchers to address particular issues about a medical product. These trials adhere to a certain research strategy, or protocol, created by the researcher or manufacturer [72–75].

Prior to starting a clinical trial, researchers evaluate existing data on the medication to create research questions and targets [76].

They then choose:

Who is eligible to participate? (Eligibility Requirements) How many participants will there be in the study?

How long the investigation will last
The existence of a control group and other measures to prevent study bias How and at what dosage the medication will be administered to patients What tests will be performed, when they'll happen, and what information will be gathered? How will the data be examined and analyzed?
Followed by clinical trials-

a) Phase 0-[77-78]

First-in-human exploratory studies that were carried out in compliance with the FDA's 2006 Guidance on Exploratory have just been given the classification of phase 0. Phase 0 studies are distinguished by the delivery of a single, sub therapeutic dosage of the study medication to a limited group of participants (10 to 15) to acquire preliminary information on the medication's pharmacodynamics and pharmacokinetics (how the drug is processed by the body)[77].

Phase 1 (First in Humans) of phase studies -Trail Layout:
Patients: 20 to 100 healthy, normal volunteers at one location who receive no advantage from participating.
Study period: brief, ranging from a few days to many weeks or months
Open label (no comparator or placebo), uncontrolled, single or multiple doses [79–82]
Purpose:
Studies on the mechanisms of action (ADME) and PK/PD Pharmaceutical impact
Tolerance, adverse reactions, and toxicity at various dosages Early indications of effectiveness
Assesses safety by identifying the most probable toxicities and dose range. 70% of drugs advance to the following phase [83]

Phase 2 :[Designing the Therapeutic Exploratory Trail]

- Patients: between 100 and 300 people with the specific illness or condition
- Study period: a few months to two years
- Efficacy and negative effects
- Randomized, placebo or active control, parallel double-blind trial, single or multiple doses, multicenter
- [84] are the different research types.
- Dosage range discovery (minimum and highest effective dosage) is the goal [85].
- Effectiveness for treating the illness or condition for which the medication is prescribed;
- Maximum Tolerated Dose (MTD); Common short-term hazards and adverse effects
- Pharmacokinetics Percentage of Drugs Entering the Following Phase 33 [86].

Phase 3: Pivotal Trails Trail Design (Therapeutic Confirmatory)

- Patients: Several thousand to three thousand sufferers of the particular ailment or condition [87-88]. Study period: one to four years
- Randomized, placebo-controlled or active control, concurrent double-blind trial, multicenter Goals [89]
- ♦Efficiency (on a large scale)
- Age, rate, and gender disparities; a relative risk-benefit ratio; long-term safety information; dosing (for

labeling); and an evaluation of safety and efficacy

- Drugs that Advance to the next Phase: 25–30%
- When phase III trials are finished, an application is sent to the relevant regulatory agencies asking for authorization to sell the product, and once those regulatory bodies provide the necessary approval, the product is released into the market [91-93].

Phase 4 (Therapeutic Use Post-Marketing) Trail Planning [94]

- Patients: There are several hundred to a thousand people who have the illness or condition. Randomized, active or placebo control, multicenter research
- Purpose [95]
- Complete Quality of Life (QOL) paths
- Conduct pharmacoeconomic trials to determine whether the medicine is more effective than competing therapies.
- Long-term safety data collection - Epidemiological research for safety and further surveillance for impacts that are uncommon or unexpected
- ♦Add new dosage forms and formulations to the portfolio of products.

Conclusion-

- Drug Discovery and Drug Development is an time consuming process . It is the process which involves a number of steps and take s lots of years. New drugs are important parts of modern medicine with an emergence of diseases. Drug Development includes number of steps and various methods\Techniques such as QSAR, Docking, Pharmacophore, Combinatorial Chemistry…etc

Reference:-

1. FDA. Centre for Drug Evaluation and Research - Drug Safety
2. Priorities. 2017. Mandal S, Moudgil MN, Mandal SK. Rational drug design.
3. 3.SK Manirul Haque and Elaref S. Ratemi. Drug Development and analysis review. Journal of Pharmaceutical
4. Chemistry Journal. 2017; 50: 837-850.
5. 4.Shu-Feng Zhouand Wei-Zhu Zhong. Drug Design and Discovery: Principles and Applications. Journal of Molecules.
6. 2017; 22: 279-285.
7. 5.Joseph A. DiMasi. Ronald W Hansen, Henry G. Grabowski. The price of innovation: new estimates of drug
8. development costs. Journal of Health Economics. 2003; 22: 151-185.
9. 6.Russu WA. The Climate is Right to Accelerate New Drug Development for Neglected Diseases. Outlook
10. Emerg Drugs. 2012;1:1.
11. Subudhi BB, et al. Updates in Drug Development Strategies against Peptic ulcer. J Gastrointest Dig Syst.
12. 2016;6:398.
13. 8.Shimizu T and Nakagawa K. Novel Drug Development of the Next-Generation T790M Mutant Specific

14. Epidermal Growth Factor Receptor Tyrosine Kinase Inhibitors for the Treatment of Advanced Non-Small Cell
15. Lung Cancer. Biochem Anal Biochem. 2016;5:258.
16. 9.Zhao Y. Towards Structural Based Drug Development for Ebola Virus Disease. J Chem Biol Ther.
17. 2016;1:e101.
18. 10.Geert ER, et al. Selection Strategy of In Vivo Models for Ophthalmic Drug Development in Diabetic
19. Retinopathy. J Mol Genet Med. 2016;10:202.
20. 11.Nayeem N, et al. Gallic Acid: A Promising Lead Molecule for Drug Development. J App Pharm. 2016;8:213.
21. 12.Emmanuel A, et al. Preliminary Identification of Lactate Dehydrogenase Inhibitors towards Anticancer Drug
22. Development. J Develop Drugs. 2015;4:132.
23. 13.Elhassa GO and Alfarouk KO. Stem Cell Therapy in Drug Discovery and Development. J Pharmacovigilance
24. 2015;3:e140.
25. 14.Melchior ACB, et al. Bromodomain as New Targets in Drug Discovery. Biochem Pharmacol (Los Angel)
26. 2015;4:e176.
27. 15.Goldberg JM and Panoff J. Pediatric Oncology Drug Development: A Case Report and Pathways Forward.
28. Pediat Therapeut. 2014;4:202.
29. 16.Lu DY et al. Anticancer Drug Development, a Matter of Money or a Matter of Idea? Metabolomics.
30. 2015;5:e134.
31. 17.Prado CM, et al. New Pharmacological Targets for Asthma Drug Development. J Allergy Ther. 2014;5:170.
32. 18.Bourgailh J, et al. ViewLux™ Microplate Imager for Metabolite Profiling: Validation and Applications in Drug
33. Development. J Anal Bioanal Tech. 2014;5:185.
34. 19Lu DY and Che JY. Rethink Of Diabetes Treatment and Drug Development. Cell Dev Biol. 2014;3:e125.
35. 20.Papanastasopoulos P. Functional Imaging in Cancer Drug Development: A Mini-Review. J Med Diagn Meth;
36. 2014;3:157.
37. 21.Lee MKK and Dilq. Drug Development in Cell Culture: Crosstalk from the Industrial Prospects. J Bioequiv
38. Availab. 2014;6:096-114.
39. 22.Shengqian Wu, et al. Role of In-silico modeling in Drug Development for Inhalation Treatment. J Mol Pharm
40. Org Process Res. 2013;1:106.
41. 23.Jackson R. What can systems pharmacology contribute to drug development? Disease modelling as a

42. predictive tool. BioDiscovery 2012; 4: 4.
43. 24.Ceron-Carrasco JP, et al. Application of Computational Drug Discovery Techniques for Designing New Drugs
44. against Zika Virus. Drug Des. 2016;5:e131
45. 25.Ganesan A and Barakat K. Target fishing: a key to unlock the One-To-Many puzzle in drug discovery. J
46. Pharma Care Health Sys. 2016;3:e141.
47. 26.Valayil JM. Activation of Microbial Silent Gene Clusters: Genomics Driven Drug Discovery Approaches.
48. Biochem Anal Biochem. 2016;5: 276.
49. 27.Bueno J. Antimicrobial Adjuvants Drug Discovery, the Challenge of Avoid the Resistance and Recover the
50. Susceptibility of Multidrug-Resistant Strains. J Microb Biochem Technol. 2016;8:169-176.
51. 28.Melchior ACB, et al. Bromodomain as New Targets in Drug Discovery. Biochem Pharmacol (Los Angel).
52. 2015;4:e176.
53. 29.Thomas J. DiFeo, Ph.D. Drug Product Development: A technical review of chemistry, manufacturing, and controls
54. information for the support of pharmaceutical compound licensing activities. Journal of Drug Development and
55. Industrial Pharmacy. 2003; 29: 939-958.
56. 30.Pratibha Muntha. Drug Discovery and Development. Journal of Pharmacy and Pharmaceutical Sciences. 2016; 5:
57. 135-142.
58. 31.Nalaka Gooneratne. Overview of drug development. Academic Entrepreneurship for Medical and Health Scientists.
59. 2019; 1: 1-9.
60. 32.Agrawal P. Stem Cell Therapy in Drug Discovery and Development. J Pharmacovigilance. 2015;3:e140.
61. 33.Zambon S, et al. Development of a Rapid and Cost Effective Assay for the Screening of Reversible
62. Cytochrome P450 Inhibition in Parallel with Cyp3a4 Metabolism-Dependent Inhibition Using Recombinant
63. Proteins. Pharm Anal Acta. 2015;6:389.
64. 34.Xiong J. Multiple Targeting Routes of MicroRNA-22 Inform Cancer Drug Discovery. Gene Technol.
65. 2015;4:e114.
66. 35.Sanaki T, et al. Improvements in the High-Performance Liquid Chromatography and Extraction Conditions
67. for the Analysis of Oxidized Fatty Acids Using a Mixed-Mode Spin Column. Mod Chem appl. 2015;3:161.
68. Baig MH, et al. Drug Discovery and In Silico Techniques: A Mini-Review. Enz Eng. 2015;4:123.
69. Tyagi AK and Prasad S. Drug Discovery Inspired by Mother Nature for Cancer Therapy. Biochem Physiol.

70. 2015;4:e128.
71. Dembitsky VM. Astonishing Diversity of Natural Peroxides as Potential Therapeutic
72. Agents. J Mol Genet
73. Med. 2015;9:163.
74. Den Haan HD, et al. Application of Modern Drug Discovery Techniques in the Context of Diabetes Mellitus
75. and Atherosclerosis. Drug Des. 2015;4:e125
76. Marjeta U. Chemo Proteomics, a Valuable Tool for Biomarker and Drug Discovery. Mol Biol. 20143:e117.
77. 4Nazem A. Alzheimer's Disease Drug Discovery is Misled by Wrong Animal Models . J Gerontol Geriat Res.
78. 2014;3:e127.
79. .Bueno J. Biosensors in Antimicrobial Drug Discovery: Since Biology until Screening Platforms. J Microb
80. Biochem Technol. 2014;S10:002.
81. .Helieh S. Oz. Toxoplasmosis, Pancreatitis, Obesity and Drug Discovery. Pancreat Disord Ther. 2014;4:138.
82. Agrawal P. Drug Discovery and Development: An Insight into Pharmacovigilance. J Pharmacovigilance.
83. 2014;2:e120.
84. .Li Y and Yang ST. Advances in Human Pluripotent Stem Cells for Regenerative Medicine and Drug
85. Discovery. J Tissue Sci Eng. 2014;5:e127.
86. .Mishra NK and Shukla M. Application of Computational Proteomics and Lipidomics in Drug Discovery. J
87. Theor Comput Sci. 2014;1:105.
88. .Feng Y and Wang N. The New Generation of Drug Discovery and its Analytical Technologies. J Bioequiv
89. Availab. 2013;5:e42.
90. Ravindran S, et al. Significance of Biotransformation in Drug Discovery and Development. J Biotechnol
91. Biomaterial. 2012;S13:005.
92. Gupta D. Pharmacogenomics in Drug Discovery and Development. J Develop Drugs. 2013;2:e126.
93. Pradeep KV, et al. Importance of ADME and Bioanalysis in the Drug Discovery. J Bioequiv Availab.
94. 2013;5:e31.
95. Baumeister AA, et al. On the Exploitation of Serendipity in Drug Discovery. Clin Exp Pharmacol.
96. 2013;3:e121.
97. Cheng SB. The Nervous System: An Ideal Therapeutic Target for Anti-Schistosomal Drug Discovery. Tropical
98. Medicine & Surgery. 2013;1:e103.
99. Ravindran S, et al. Significance of Biotransformation in Drug Discovery and Development. J Biotechnol
100. Biomaterial. 2012;S13:005.

101. 54.Bhakta S. An Integration of Interdisciplinary Translational Research in Anti-TB Drug Discovery: Out of the
102. University Research Laboratories to Combat Mycobacterium tuberculosis. Mol Biol. 2013;2:e108.
103. 55.Pomin VH. Current Status of Fucanomics and Galactanomics in Drug Discovery and Glycomics. J Glycobiol.
104. 2013;2:104.
105. 56.Cheng F and Vijaykumar S. Applications of Artificial Neural Network Modeling in Drug Discovery. Clin Exp
106. Pharmacol. 2012;2:e113.
107. 57.Deshmukh R. Modeling and Simulation in Drug Discovery and Development. J Bioequiv Availab. 2012;4:
108. 27-28.
109. 58.Persaud-Sharma V and Zhou SF. Drug Repositioning: A Faster Path to Drug Discovery. Adv
110. Pharmacoepidem Drug Safety. 2012;1:e117.
111. 59.Sánchez HEP. Exploitation of Massively Parallel Architectures for Drug Discovery. Drug Des. 2012;2:e108.
112. 60.Young W, et al. Patientspecific Induced Pluripotent Stem Cells as a Platform for Disease Modeling, Drug
113. Discovery and Precision Personalized Medicine. J Stem Cell Res Ther. 2012;S10:010.
114. 61.Yang Z and Marotta F. Pharmacometabolomics in Drug Discovery & Development: Applications and
115. Challenges. Metabolomics. 2012;2:e122.
116. 62.Patil SA. Role of Medicinal Chemist in the Modern Drug Discovery and Development. Organic Chem Curr
117. Res. 2012;1:e110.
118. 63.Medina-Franco JL. Drug Discovery with Novel Chemical Libraries. Drug Des. 2012;1:e105.
119. 64.Liu Y. Renaissance of Marine Natural Product Drug Discovery and Development. J Marine Sci Res Development. 2012;2:e106.
120. 65.Gonzalez-Sabin J. Natural Products: Back to the Future in Drug Discovery. Biochem Pharmacol (Los Angel)
121. 2012;1:e112
122. 66.Pascu ML. The Laser Use in Generating New Species of Medicines with Antitumor and Antibacterial
123. Properties: New Processes in Drug Discovery. Biochem Pharmacol (Los Angel). 2012;1:e111.
124. 67.Elzahabi HAS. Virtual Screening in Drug Discovery, A Topic between Believe and Reality? Biochem
125. Pharmacol (Los Angel). 2012;1:e103.
126. 68.Nishant T, et al. Role of Pharmacokinetic Studies in Drug Discovery. J Bioequiv Availab. 2011;3:263-267.
127. 69.Celikyurt IK. Thought-provoking Molecules for Drug Discovery: antioxidants. Pharm Anal Acta.
128. 2011;S3:001.
129. 70.Fortuna A, et al. In vitro and In vivo Relevance of the P-glycoprotein Probe Substrates in Drug Discovery and

130. Development: Focus on Rhodamine 123, Digoxin and Talinolol. J Bioequiv Availab. 2011;S2.
131. 71.Torzewski J, et al. Road Map to Drug Discovery and Development–Inhibiting C-reactive protein for the
132. Treatment of Cardiovascular Disease. J Bioequiv Availab. 2011; S1:001.
133. 72.Arun B. Challenges in Drug discovery: Can We Improve Drug Development. J Bioanal Biomed. 2009;1:050-053.
134. 73.Subudhi BB, et al. Updates in Drug Development Strategies against Peptic ulcer. J Gastrointest Dig Syst.
135. 2016;6:398.
136. 74.Zhao Y. Towards Structural Based Drug Development for Ebola Virus Disease. J Chem Biol Ther.
137. 2016;1:e101.
138. 75.Ashok Kumar Panda. Ayurveda Treatment Outcomes for Osteoarthritis. J Homeop Ayurv Med.
139. 2015;4:e115
140. 76.Jayram H, et al. Ayurvedic Regimen in Hemorrhagic Ovarian Cyst without Peritoneal Bleeding: A Case
141. Report. J Homeop Ayurv Med. 2014;3:164
142. 77.SB Thorat, SK Banarjee, DD, Gaikwad SL, Jadhav RM, Thorat. Clinical Trial: A Review. International Journal of
143. Pharmaceutical Sciences Review and Research. 2010; 1: 101-106.
144. 78.The Lancet, Phase 0 trials: a platform for drug development? Lancet 2009; 374: 176
145. 78.Panda AK. Complementary and Alternative Medicine is Mother Medicine. Altern Integr Med. 2013;3:e112.
146. 79.Hazra J and Panda AK. Concept of Beauty and Ayurveda Medicine. J Clin Exp Dermatol Res. 2013;4:178.
147. 80.Shintani H. Drug Development and Validation. Pharmaceut Anal Acta. 2013;4:e149.
148. 81.Huang L. Inhibiting Protease Auto-processing: A Novel Strategy for Anti-HIV-1 Drug Development. Biochem
149. Physiol. 2013;2:e115.
150. 82.Aliev G, et al. Mitochondria Specific Antioxidants and their Derivatives in the Context of the Drug
151. Development for Neurodegeneration and Cancer. Drug Des. 2013;2:103.
152. 83.Sun L. Peptide-Based Drug Development. Mod Chem appl. 2013;1:e103
153. 84.Sun L. Peptide-Based Drug Development. Mod Chem appl. 2013;1:e103.
154. 85.Amin A and Lowe L. Plant-Based Anticancer Drug Development: Advancements and Hurdles. J Gastroint Dig
155. Syst. 2012;2:e111.
156. 86.Elsheikha H and Rauch CRedefining the Limits of Biochemistry in Multidrug Resistant Nematodes:
157. Implications for Future Drug Development. J Vet Sci Technol. 2012;3:e110.
158. 87.Bhattacharyya S. Application of Positron Emission Tomography in Drug Development. Biochem Pharmacol.
159. 89.Luisa BM, et al. Challenges Faced in the Integration of Pharmacogenetics/Genomics into Drug Development. J Pharmacogenomics Pharmacoproteomics. 2012;3:108.
160. 90.Panda AK. Evidence based Ayurveda Practice. J Homeop Ayurv Med. 2012;1:e108.

161. 91.Ansari R. Defining the Role of Single Nucleotide Polymorphic (SNP) in Drug Development and Toxicity. J
162. Drug Metab Toxicol. 2012;3:e103.
163. 92.
164. Kummalue T. Difficulties of Drug Development from Thai Herbal Medicine. Pharm Anal Acta.
165. 2012;S15:002.
166. 93.Khan A and Khan AU. Biomarker Discovery and Drug Development: A Proteomics Approach. J Proteomics Bioinform. 2012;5: 5-6.
167. 94.Sang N. Biochemistry, Drug Development and Open Access. Biochem Pharmacol. 201;1:e101.
168. 95.Nicolson TJ, et al. The Post-Transcriptional Regulator EIF2S3 and Gender Differences in the Dog: Implications for Drug Development, Drug Efficacy and Safety Profiles. J Drug Metab Toxicol. 2010;1:101.
169. 96.Source: Raval K, Ganatra T. Basics, types and applications of molecular docking: A review. IP Int J Comprehensive Adv Pharmacol
170. 2022;7(1):12-16.
171. 97. Yang et al., 2010, Drug Discovery Today, 15(11), 444-450. Doi:
172. 98.Muhammed and Akı-Yalçın, JOTCSA. 2021; 8(3): 749-762.
173. 99.Qing et al. Journal
174. of Receptor, Ligand and Channel Research. 2014;7:81-92
175. 100) C.A. Lipinski, F. Lombardo, B.W Dominy, P.J. Feeney, Experimental and computational approaches to estimate solubility and permeability in drug discovery and drug development settings. Adv. Drug. Delivery Rev. 23,4-25(1997).
176. 101) D.F. veber, S.R. Johnson, H.-Y. Cheng, B.R. Smith, K.W. Ward, K.D. Kopple, Molecular properties that influence the oral bioavailability of the drug candidates.J.Med.Chem.45, 2615-2623(2002).