E-ISSN: 2278-3229

IJGHC, June 2021 –August, Sec.B; Vol.10, No.3, 215-220.
DOI: 10.24214/IJGHC/HC/10/3/21520.

International Journal of Green and Herbal Chemistry

An International Peer Review E-3 Journal of Sciences

Available online at www.ijghc.com

Section B: Herbal Chemistry

Research Article

CODEN (USA): IJGHAY

Drug Repurposing and Traditional Drug Discovery: An Overview

Kavita Chahal[1] and Twinkle Solanki[2]

[1]Department of Botany, Government College Bichhua, Chhindwara, (M.P.) India

[2]Department of Chemistry, Government College Bichhua, Chhindwara, (M.P.) India

Received: 30 May 2021**; Revised:** 07 June 2021; **Accepted:** 17 June 2021

Abstract: In the present scenario when both simple and life-threatening infectious diseases are increasingly becoming an attractive proposition, there is an urgent need for new treatments against the causative agents like bacteria, fungi and viruses. The aim of this review is to provide an overview of the various aspects of repurposing of a drug in comparison to the traditional drug production system. It will give a general view about the manufacturing process, present approaches, and opportunities used for the traditional drug processing and for drug repurposing.

Keywords: Life-Threatening, Drug Repurposing, Approaches, Challenges

INTRODUCTION

As we are witnessing the recent pandemic of dangerous microbial pathogens, and also aware of the fact that despite the recent advances in antimicrobial treatments, most infections lack specific treatment. Many of the recent therapeutic strategies failed to cope with the re-emergence and mutations in microbes [1]. There is an urgent need to study these mutations thereby improving our knowledge of disease and defence mechanisms in order to identify new therapeutic molecules using a pool of potential pharmacological targets [2], and to repurpose the existing drugs. In such case, to a great extent, drug

repurposing combined with some innovative approaches is proving to be an effective therapeutic strategy as compared to the traditional system of drug production [3].

2. MATERIALS AND METHODS

2.1. Traditional system of drug production: Plants have been the source of drugs for the treatment of various diseases since time immemorial. The phytochemicals and secondary metabolites from plants have been proved to contain various activities like antimicrobial, antioxidant, anti-inflammatory, immunomodulatory potential and many more [4].

2.2. Repurposing of a drug: Drug repositioning or drug reprofiling or re-tasking is the procedure of reusing an already known, approved, discontinued, shelved or experimental drugs that have already proven to be safe and effective in experimental animals and humans. It is also known as indication expansion or indication shift or rescuing and therapeutic switching, as it involves change or shift of its medical uses [5]. Repurposing of a drug helps to increase the identification and classification of those already existing drugs that have potential to cure or prevent viral infections. For instance, an antiviral amantadine which was originally used to treat influenza was then repurposed to be used in treating Parkinson's disease [6]. The principle of mechanism of drug repurposing lies in the fact that the same molecular pathways may be involved in different diseases [7].

2.3. Methodology for Traditional Plant derived drugs: The development of new plant derived medicines is very time consuming and complex process. It takes approximately 12 years from selecting a plant, drug extraction, discovery of a new drug to reaching the medical shop [8,9].

2.3.1. Survey and selection of plants***:*** There are five major approaches for the selection of plants, which are:

- ***Random approach:*** this is based only on observation based on morphological features without having knowledge and experience about the selected plants. it involves collecting all the available plants in a particular area.
- ***Taxonomic approach:*** this is based on the taxonomic features about a particular plant that is to be studied. It involves the knowledge of specific genus or family and their possible locations.
- ***Phytochemical or chemotaxonomic approach:*** this is based on the knowledge of bioactive chemical type in order to treat a particular disease.
- ***Ethno-medical approach:*** this is based on the prior knowledge of a particular plant and its medicinal use in different areas.
- ***Information-managed approach:*** this is based on information, about their usage and activity of plants, collected from local areas after doing a detailed survey.

2.3.2. Isolation, identification, and characterization of phytochemicals: it includes many Phytochemical screening assays includes tests for carbohydrates, tests for proteins, tests for amino acids, tests for steroid and triterpenoid, tests for glycosides, tests for flavonoids, tests for alkaloids, tests for tannins and phenolic compounds [10].

2.3.3. Extraction or bio-fractionation of plant materials collected: It is then isolated with chromatographic separation, purification, and new phytoconstituents having good bioactivity are characterized. The different chromatography techniques are thin layer chromatography (TLC),

DOI: 10.24214/IJGHC/HC/10/3/21520.

High performance thin layer chromatography (HPTLC), Column chromatography (CC), and High-performance liquid chromatography (HPLC).

1. Methods of detection of compounds or functional groups (chemical bonds) present in an unknown mixture of plant extracts includes Mass spectrometry (MS), Fourier-transform infrared spectroscopy (FTIR), Nuclear magnetic resonance spectroscopy (NMR), High-throughput screening (HTS). This a specially designed technique and a standard method based on identification through stored libraries [11].
2. Designing of new analogues: newly isolated phytoconstituents are used as lead compounds having improved therapeutic activity. This is followed by production of final drugs by R & D with socioeconomic benefits, to be used by common people [12].

2.4. Methodology for Drug Repurposing: When the economy doesn't favour the development of novel drugs and when there is an urgent need of an effective drug, drug repurposing is particularly an attractive approach for rare and neglected conditions [13].

The major approaches followed in drug repurposing are:

1. Approach based on clinical or experimental research gives a direct evidence of links between drugs and diseases to be developed, that are reliable and credible. Some of them are target screening approaches cell assay approaches, animal model approaches and clinical approaches. High throughput phenotypic screening of drugs with in-vitro or in-vivo animal models for a particular disease reflects the potential for clinical evaluation. The new targets have to be identified by affinity chromatography and mass spectrometry just like the traditional approaches of plant derived drugs [14].
2. Approach based on computational research involves the use of networking and digital libraries like the retrospective clinical analysis of surveillance data. The novel targets can also be identified by network analysis involving the known data of genes and proteins. Signature matching in which a particular characteristic (transcriptome or structure of effect) of a drug is to be compared with the same characteristic of another drug. Structure based Molecular docking computational approach involving the binding site complementarity between a drug (ligand) and a viral protein (therapeutic target). In precision medicine approach, in addition to environment, and lifestyle for each individual, separate variability in genes is considered. The treatment depends on variations in an individual's genome, transcriptome, proteome, and metabolome, or to specific types of a general condition. The systems medicine network control analysis is used to design a combination of several drugs that work in a synergistic manner, also called as multitarget therapeutics. The synergism has advantages of easier administration, shorter duration of treatment, lower dose requirement and more protection against the emergence of resistant parasites. High throughput cell-based screening methods, *in-vivo* and *ex-vivo* bio-analytics, and database-driven bioinformatics approaches are another computational approach [15].
3. Mixed approaches: to find out more effective ways of treatments in the present scenario of life-threatening diseases, researchers have combined computational approaches and experimental approaches to find new indications for drugs. This is called as mixed approaches, wherein the result of computational methods was validated by biological experiments and clinical tests. It offers more opportunities for developing repositioned drug effectively and rapidly [16].

3. RESULT AND DISCUSSION

3.1. The pathway of repurposing drug: Identification and screening of repositioning drugs involves about two years. For about 1-2 years, desired compound is identified from approved drug libraries. Drugs or candidates or the lead compound chosen for repurposing includes the drugs in clinical development that failed to deliver efficacy during clinical trials, or those with no major safety concerns, or those that are being discontinued for commercial reasons, or those half-baked drugs from academic institutions and public sector laboratories. These are called as the Pharmacophore whose features are directly responsible for activity. The structural features are optimized in order to improve interactions with the target. 1-6 years are spent in clinical trials where experimental models are used to determine toxicity and efficacy of the drug. The effect of drug on humans and vice versa i.e., Pharmacodynamics and Pharmacokinetics of the drug are determined. Next 1-2 years are involved in completing the registration, patenting and marketing of the finally examined drug [17].

3.2. A comparative pathway of traditional drug development and drug repurposing has been shown here in figure 1

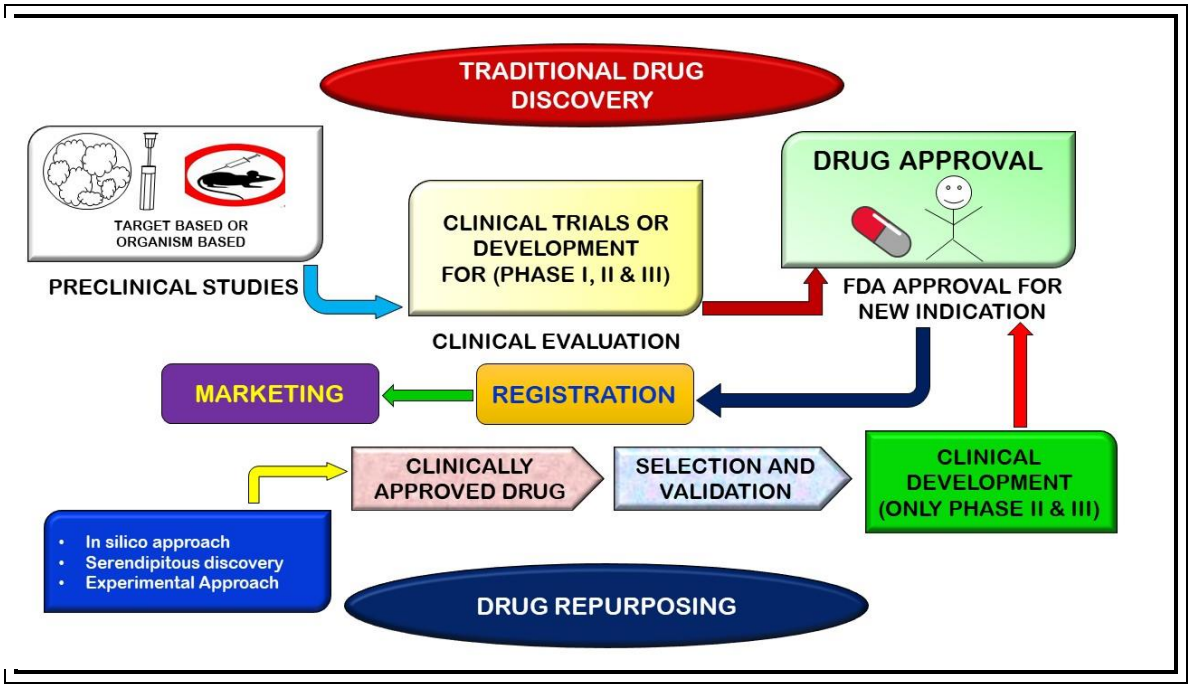

Figure 1: An overview of pathways followed by traditional drug development and drug repurposing

3.3. Advantages of drug repurposing over traditional drug development process: There have been many disadvantages associated with the traditional drug discovery system. The discovery of novel drugs based on plants is a time taking and a challenging task for designing new lead compounds [18]. The average cost of introducing one new traditional plant-based drug to the market in developed countries, including the cost of failures, has been estimated to be near billions. It involves a detailed procedure starting from survey for the selection of plants using the five approaches, to its phytochemical analysis, characterization and pharmacological investigation [19]. Consequently, the current procedure of traditional drug discovery is ill-equipped to fight against rapidly emerging and re-emerging infectious diseases, such as mutated and drug-resistant strains of viruses, and other infectious microorganisms.

DOI: 10.24214/IJGHC/HC/10/3/21520.

Other drawbacks being the cost, time consumption, and risk-prone venture. Also, the productivity problem, worldwide pressure on economy, competition from generics, and ever-increasing regulatory challenges, has driven many drug companies to become more innovative in finding new uses for existing drugs by relying on the more effective and advantageous drug repurposing system [20].

4. CONCLUSION

In order to bring new and much effective drugs into the pharma market, drug repurposing of traditional plant-based drugs has shown to offer faster and cheaper ways of treating both common and rare diseases. Research and Development sectors also has found it far better, that can overcome all those disadvantages associated with the traditional de novo drug synthesis. This scientific approach of finding and discovering new and more potent drug compounds is an urgent need of present scenario of life-threatening diseases.

REFERENCES

1. S.S.Wong and K.Y.Yuen, Streptococcus pyogenes and re-emergence of scarlet fever as a public health problem, 2012. 1, Available: http://www.ncbi.nlm.nih.gov/pubmed/26038416
2. B.Chopra and A.K.Dhingra, Natural products: A lead for drug discovery and development, 2021. Available: http://www.ncbi.nlm.nih.gov/pubmed/33847440
3. H.Pekel and M.Ilter and O. Sensoy, Inhibition of SARS-CoV-2 main protease: a repurposing study that targets the dimer interface of the protein, 2021.Available: http://www.ncbi. nlm.nih. gov / pubmed / 33847241
4. L.I.U. Dan, Construction of multiple drug release system based on components of traditional Chinese medicine, China Journal of Chinese Materia Medica, 2012. Available: http://dx.doi.org /10.4268 /cjcmm20121531
5. Y.Cha and T. Erez,I.J. Reynolds, D. Kumar, *et al.* Drug repurposing from the perspective of pharmaceutical companies, 2018. 175. Available: http://www.ncbi.nlm.nih .gov/pubmed /28369768
6. L.H.Jones and M.E.Bunnage, Applications of chemo genomic library screening in drug discovery, 2017. 16. Available: http://www.ncbi.nlm.nih.gov/pubmed/28104905
7. Pushpakom, Sudeep, *et al*. "Drug repurposing: progress, challenges and recommendations." Nature Reviews Drug Discovery, 2019, 18, 1, 41+.
8. H.Ti, Z.Zhuang, Q.Yu and S.Wang, Progress of Plant Medicine Derived Extracts and Alkaloids on Modulating Viral Infections and Inflammation, 2021, 15, .Available: http://www.ncbi.nlm.nih. gov/ pubmed /33833499
9. D.Lobine, N. Sadeer, S. Jugreet *et al.* Potential of medicinal plants as neuroprotective and therapeutic properties against amyloid-β-related toxicity, and glutamate-induced excitotoxicity in human neural cells, 2021 .Available: http://www.ncbi.nlm.nih.gov/pubmed/33845746
10. Showkat R. Mir, Tara Fuad Tahir, Javed Ahamad, Raad A Kaskoos, Naila Hassan Ali Alkefai, Abdul Samad, Spectroscopic Techniques for the Structural Characterization of Bioactive Phytochemicals, Bioactive Phytochemicals, 2020, Drug Discovery to Product Development, pp. 73-99. Available: http://dx.doi.org/10.2174/9789811464485120010008

11. Donghao Li, Han Yeong Kaw, Xiangzi Jin, Extraction of Plant Materials, Liquid-Phase Extraction,2020, pp. 667-682. Available: http://dx.doi.org/10.1016/b978-0-12-816911-7.00022-0

12. Sumira Jan, Nazia Abbas, 2018, Chemistry of Himalayan Phytochemicals, Himalayan Phytochemicals, 2018,121-166. Available: http://dx.doi.org/10.1016/b978-0-08-102227-6.00004-8

13. Alkesh kumar Patel, Drug Repurposing in Oncotherapeutics, Drug Repurposing - Hypothesis, Molecular Aspects and Therapeutic Applications,2020, Available: http://dx.doi.org/ 10.5772/ intechopen.92302

14. Enrique Hernández-Lemus, A personalized medicine approach to drug repurposing for the treatment of breast cancer molecular subtypes, Drug Repurposing in Cancer Therapy,2020, pp. 191-211. Available: http://dx.doi.org/10.1016/b978-0-12-819668-7.00007-5

15. Megan Golden, Jabe Wilson, A Network Medicine Approach to Drug Repurposing for Chronic Pancreatitis, 2020. Available: http://dx.doi.org/10.1101/2020.10.30.360263

16. Kai Zhao, Hon-Cheong So, Using Drug Expression Profiles and Machine Learning Approach for Drug Repurposing, Methods in Molecular Biology, Computational Methods for Drug Repurposing,2018, 219-237.Available: http://dx.doi.org/10.1007/978-1-4939-8955-3_13

17. Sohini Chakraborti, Pushpaveni Chakravarthi, Narayanaswamy Srinivasan, A ligand-centric approach to identify potential drugs for repurposing, Drug Repurposing in Cancer Therapy,2020, pp. 15-54. Available: http://dx.doi.org/10.1016/b978-0-12-819668-7.00002-6

18. Bei Cheng, Peisheng Xu, Nanoparticle-based formulation for drug repurposing in cancer treatment, Drug Repurposing in Cancer Therapy,2020, pp. 335-351.Available: http://dx.doi.org/10.1016/b978-0-12-819668-7.00013-0

19. Hermann A.M. Mucke, 2015, A New Journal for the Drug Repurposing Community, Drug Repurposing, Rescue, and Repositioning,2015,1,1,3-4. Available: http://dx.doi.org /10.1089 /drrr. 2014. 0002

20. R.Varanasi, D. Nayak and A. Khurana, Clinical Repurposing of Medicines is Intrinsic to Homeopathy, 2021. Research Initiatives on COVID-19 in India. Available: http://www.ncbi. nlm.nih. gov /pubmed/33853178

***Corresponding Author: Kavita Chahal,**

[1]Department of Botany, Government College Bichhua, Chhindwara, M.P 480111

Online publication Date: 20.06.2021