IJNRD.ORG ISSN : 2456-4184
INTERNATIONAL JOURNAL OF NOVEL RESEARCH AND DEVELOPMENT (IJNRD) | IJNRD.ORG
An International Open Access, Peer-reviewed, Refereed Journal

DRUG REPURPOSING IN THE MODERN ERA: OPPORTUNITIES, CHALLENGES AND FUTUREDIRECTIONS

[1]Mr. Tejas V. Fendar, [2]Miss. Sanskruti R. Jamode, [3]Dr. Akshay M. Kasambe, [4]Mr. Dhiraj D. Mangam, [5]Dr. Avinash S. Jiddewar

[1]Student, [2]Student, [3]Associate Professor, [4]Assistant Professor, [5]Principal [1]Navsanjeevan Shikshan Mandal's College of Pharmacy Darwha, Yavatmal, India

Abstract: Drug repurposing, the process of identifying new therapeutic uses for existing drugs, has become an increasingly popular strategy in the pharmaceutical industry and in the academy. In recent years, advances in bioinformatics, big data and artificial intelligence have significantly expanded the possibilities of drug repurposing. Enabling the discovery of new indications through in silico methods, biological screening and real-world data analysis. This approach provides significant advantages, including reduced development time, lower costs, and potentially higher success rates because existing drugs have already undergone various safety evaluations. Despite these benefits, challenges such as intellectual property issues, regulatory hurdles, and limited knowledge about mechanisms of action may hinder progress. In addition, the repurposing of drugs often requires a strong collaboration between different disciplines, which can be logistically complex. This review reviews the current landscape of drug repurposing, highlightsthe most promising techniques, discusses key challenges, and suggests future directions to maximize the impact of this approach inmodern drug development.

Keywords **- Drug repurposing, Drug repositioning, COVID-19 drug repurposing, Clinical trial, Artificial Intelligence in Drug repurposing, Data base, Regulatory challenge in drug repurposing, Future of Drug repurposing etc.**

I. INTRODUCTION

Drug repositioning occurs in the context of repositioning an active pharmaceutical ingredient which is currently advertised for a new proposal. Despite the fact that this technique has a number of disadvantages and there are some challenges, it also has many advantages, including changes to overcome the constant loss currently observed in the field of new drug discovery [(1)] The history of pharmaceutical products is marked numerous cases of repositioned drugs, including a number of extremely old medication. Most of them are out by chance. New strategies have been created, based on data mining specific, to identify new candidates for drug repositioning. Some startups have dedicated entirely to the development of this concept, and a mag- azine is (Drug use, rescue andrelocation; MA Liberty Inc., Boston, MA, USA), as well as an annual international conference (8th edition was held in WashingtonDC in 2019). This article provides a detailed overview reuse and highlight in particular its latest scientific premises and ultra- modern tools, especially IT, is used to make them more efficient. The approval process for a recent drug it is expensive and can take10 to15 minutes [(2).] This long discovery process opens the door to drug repurposing (repositioning) as an approach essential to reduce the time needed to produce a medicine. Drug repurposing involves the use of drugs approved by administrative agencies such as the FDA, the European Medicines Agency (EMA), the Medicines and Healthcare products Regulatory Agency (MHRA), among others, for a more re- cent suggestion. Because of its great promise shorten the improvement cycle, many pharmaceutical companies now they are starting to repurpose drugs to recover many of them duct patches approved by the FDA and initially unprofitable as new therapies for various diseases The exposure analysis provides an illustration of the approach currently used forrepurposing and reviews case studies that illustrate the control and utility of drug repurposing observed by significantly reducing the time required to produce a drug for via the availability of all applicable clinical and toxicological data[(3)] . Various approaches to reuse and related challenges are discussed in this composition. Developing new drugs takes time and is expensive.

According to Employee Research Group[(4)] usually receives from 10 to15 times and from 0.8 to 1.5 billion. dollars to develop a drug candidate, while the success rate for the development of a new molecular reality is only 2.0[(5)] Effective identification of news signals from approved or well-established clinical medication essential role in drug discovery. [(6,7,8)] Such a process is also known

repositioning or reprofiling the drug and can bypass several pre-approval tests required for therapeutic compounds of little development. In general, Drug repositioning offers a number of benefits during the process drug discovery, such as less risk of failure, low investment and shorter development times. [9,10] Connect small patches that can lead to a review of biochemical mechanisms through interactions with special natural targets was the crucial prospect of discovery recent drug discovery (DD). This idea revolutionized the DD channel, comes in expansion advancement of combinatorial chemistry and HTS over the past many decades. In any case, these styles include veritably high costs and long assay development and standardization times, which aren't reasonable for all. In this situation, a shift from conventional ways of synthesizing and screening huge chemical libraries to the conception of drug repositioning/ repurposing (DR), in which medicines with known suggestions are aimed for ultramodern suggestions, is a safe and less expensive alternative. This fast medicine development methodology includes the evaluation of new illness pathways, relating ultramodern targets and studying their structures, functions, and elements to typically reposition suitablemotes from the given chemical space, or maybe than random screening. [11,12]

In silicon DR has attracted the recommendation of the pharmaceutical companies and research communities world-wide during the current COVID- 19 wide since the use of advanced computational algorithms can predict 3D structures of targets, identify authoritative pockets commerce hotspots of new drug targets, and screen the known drug candidates against new target structures,significantly reducing the time and cost needed for DR.1DR includes the identification of new operations for being drugs at a lowercost and in a shorter time.[13]

There are different computational DR ways. For illustration, computational DR approaches that have been applied to the COVID-19 epidemic can be astronomically distributed into

(i) drug/target network-based models
(ii) structure-based approaches
(iii) AI based approaches.

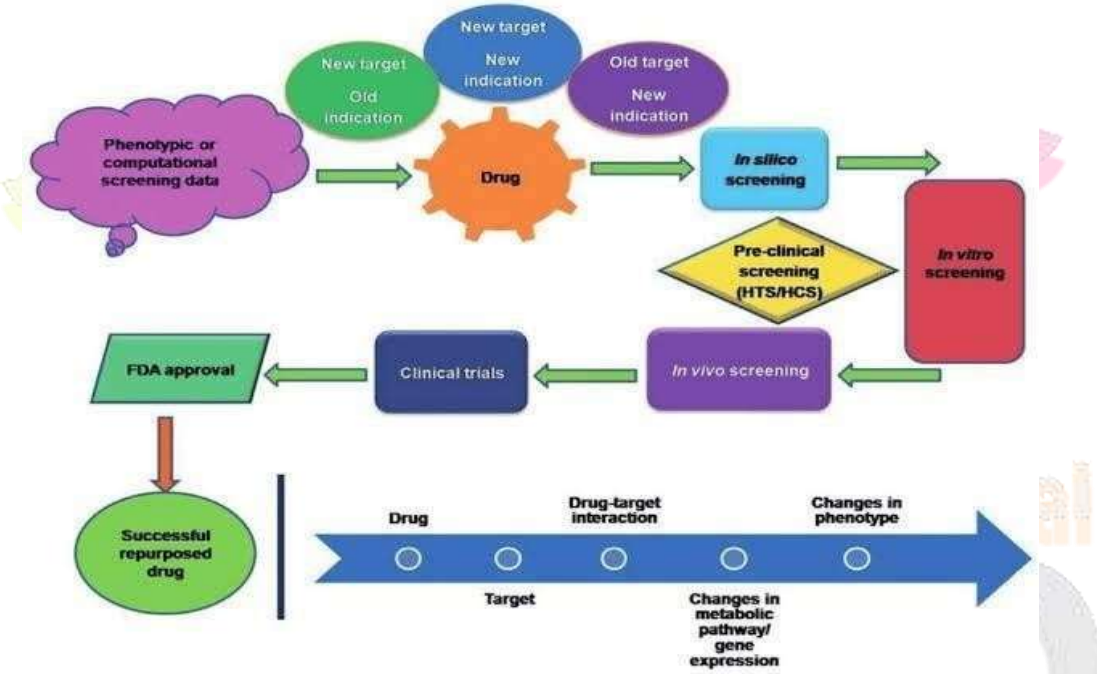

fig.1 overview of drug repurposing.

II. SIGINIFICANCE OF DRUG REPURPOSING

The Drug repositioning has attracted considerable attention for its potential to discovery new uses for existing drugs and to create new drugs in pharmaceutical companies and industry, due to its effectiveness in saving time and cost. compared to the conventionalapproach for the development of new medicines [14]. Drug repurposing is also known as drug repurposing, drug repurposing, drug repurposing and therapeutic switching. In order for a new drug to enter the market, it must undergo strict guide- lines. The identification of a drug and its development requires a critical approach, mainly due to the different physicochemical properties of chemicals and the complexity of growing production [15]. This restriction allows pharmaceutical companies or centers Scientists to quickly and effectively use drugs already approved for a signal not used, without being available to patients suffering from this disease. Experimental particles that cannot test their stability for the default signal usually gives a good start to rebuild them by reusing them.

They may be found for one or more long-term modern indications to be developed as practical treatments, especially useful in casesof rare diseases, which present critical challenges in terms of definition, treatment and resource requirements [14]. For example, some immune system disorders, bacterial infections and rare cancers are not acquired, which makes them more difficult to treat becausethey are idiopathic in nature [15]. Drug reuse, being a less expensive and shorter approach, provides effective treatments for patientscompared to conventional (traditional) forms of discovery and development. expanding, this approach helps to overcome the

increasing costs of improving medicines, thereby reducing patients' out-of-pocket expenses and ultimately reducing the actual costof treatment[29].

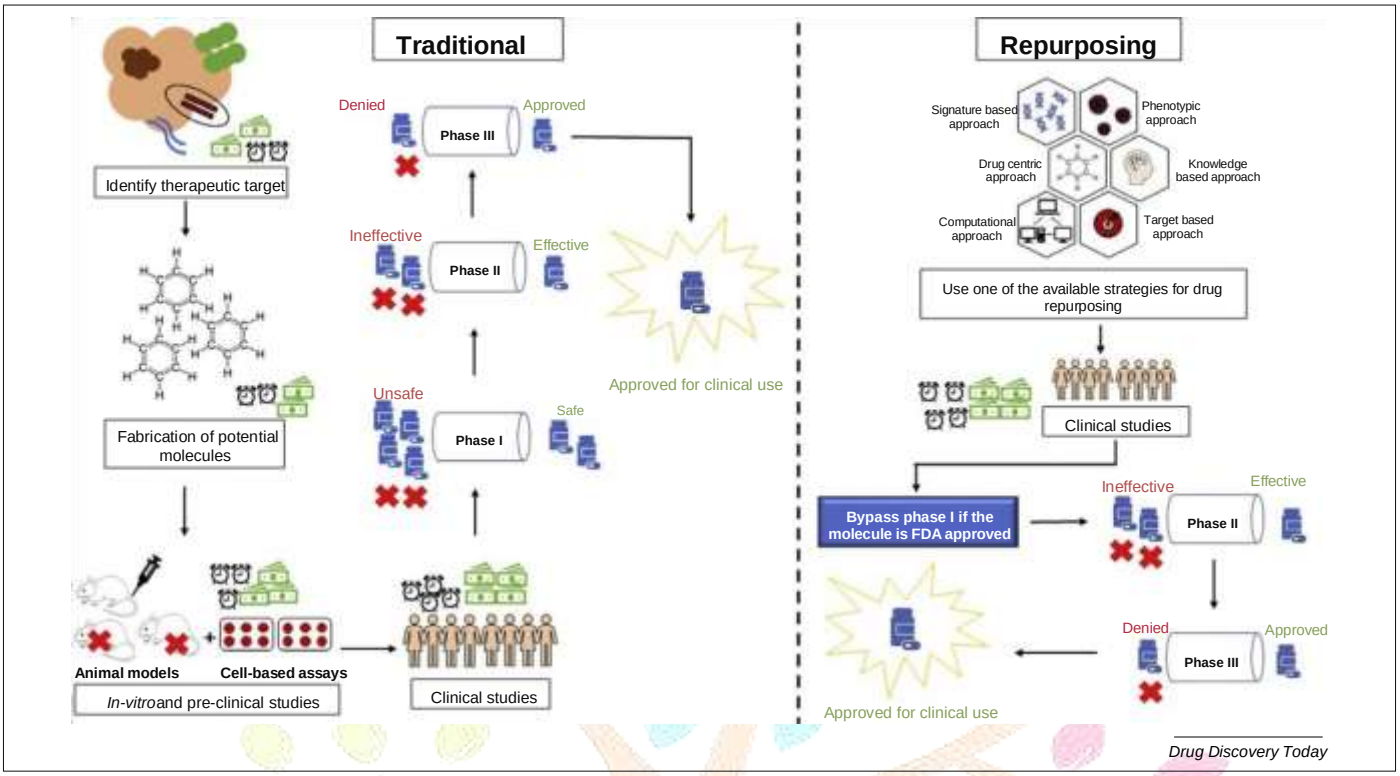

fig.2 a comparison of traditional drug discovery process versus drug repurposing. the traditional drug discovery process is time consuming and involves a large financial burden on the innovators. by repurposing a drug, precious years can be cut down from a typical drug discovery cycle. repurposing abolishes all the steps needed for FDA approval. also, once the drug is FDA approved, phase i of clinical trials can be eliminated, which saves a lot of time, effort and money involved in the studies. a short path can be followed to innovate a new system for clinical use using drug repurposing strategies

III. NOTABLE OPPORTUNITIES IN DRUG REPURPOSING

Most of the current reuse projects rely on a specific approach, which includes computational or experimental strategies or both, as recently reviewed in detail by Pushpakom [16]. Regardless, the discovery of some of the most successful cases of drug reuse was generally inadvertent and successful or is based on retrospective clinical experience. Two of the most notable cases are thalidomideand sildenafil citrate.

No.	Drug name	Original indication	New indication	Mechanism of action	Status of study	Ref.
1.	Aspirin	Fever and pains	Melanoma	The growth of the cells tumors in blocked otheruse enzymes necessary cell growth	PhaseII	17
2.	Minoxidil	Antihypertensive	Hair regrowth	This stimulate follicular movements	Approved	18
3.	Raloxifene	Osteoporosis	Breast cancer	Effect of antagonist of estrogen	Approved	18
4.	Tamoxifen	Breast cancer	Bipolar disorder	Anti estrogen	Approved	18
5.	Thalidomide	Morning sickness	MultipleMyeloma	Antiangiogenic	Approved	19
6.	Sildenafil	Angina pectoris	Erectile dysfunction	Phosphodiesterase type 5 (PDE5) inhibition	Approved	20

table 1 -under studied repurposed drug

IV. TECHNOLOGICAL ADVANCES IN DRUG REPOSITIONING

Current research strategies related to advances in cell-based screening, multiple assays, data mining, in silico bioinformatics, and cheminformatics databases, the pharmaceutical industry has shown an increased interest in discovering compounds that have failedin development for various reasons[21].In general, there are three recent steps in this consideration of drug repositioning: (1) distinct evidence of candidate molecules for a given indication; (2) hypothetical evaluation of drug effect in preclinical models; and (3) evaluation of rescue efficacy in phase II clinical trials.

Approaches to drug repositioning can be divided into two main categories, computational and experimental approaches. Using these approaches separately or in combination, it is possible to form theories about the generation of drug candidates for repurposing. Repurposing approaches: new suggestions for a drug candidate can be combined incidentally or can be collected through reasonable approaches. Drug repurposing strategies can include experimental and computational strategies that have major implications for demonstrating the best corresponding mechanisms and pathways involved in the pathogenesis of complaints.

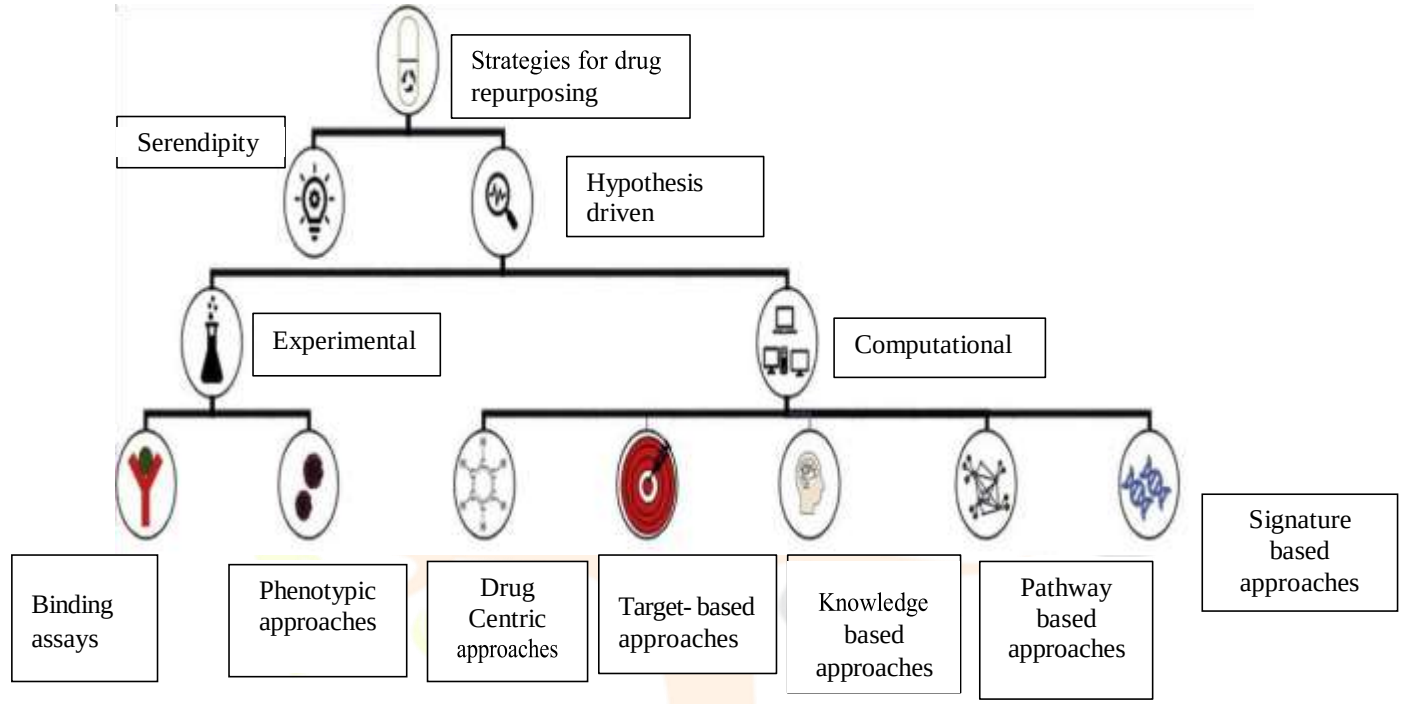

fig.3 a schematic representation of the strategies that can be used to repurpose a drug

4.1 Drug Repurposing Computational Strategies for COVID-19

Drug repurposing strategies for COVID-19 The workflow for drug repurposing is organized differently from traditional drug development. In the context of drug repurposing, there are more limited tools and different metrics to track ingredient identification, procurement, development and post-marketing safety monitoring by the Food and Drug Administration (FDA).

Computational drug repurposing approaches applied to COVID-19 can be are generally classified as

a) Network-based models,
b) structured based approaches,
c) Deep learning machine approaches [22]

.

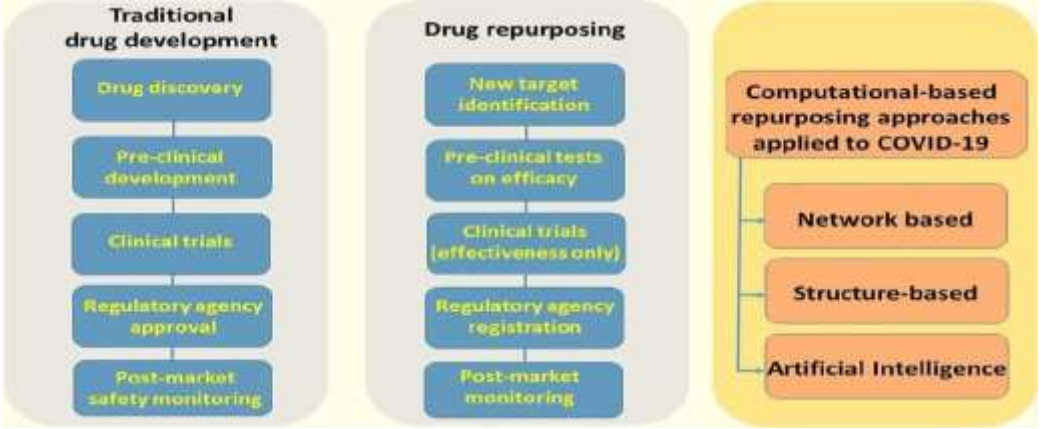

fig.4 drug repurposing compared to traditional drug development workflow and drug-repurposing approaches applied tocovid-19

V. CHALLENGES AND LIMITATIONS OF DRUG REUSE

Despite the fact that the reuse of drugs has recently gained popularity, the applications are less than expected due to various challenges related to the correct implementation. Since there is no hard and fast regulatory guidance for reporting drug candidates, it is difficult for aspiring startups to provide meaningful data to regulators. In addition, the exclusivity granted by the license and the Orphan Drug Act could theoretically apply to the use of a drug repurposed for a new use [23].

However, such exclusivity cannot prevent a doctor from using the drug off- label. There are several drugs, such as thalidomide and rapamycin, that have been subject to additional restrictions due to a sudden regulatory change that allows patients to access needed therapies at a lower cost. However, due to the lack of a clear exclusivity pathway, the use of repurposed drugs remains a significant obstacle [23]

5.1 Drug repurposing offers numerous advantages but moreover faces out- standing challenges and limitations.

In general, a candidate for repurposing carries a potential time risk, especially if it has failed for an already targeted brand. In this scenario, it is appropriate to plan a branched development program in which the lead compound or drug is evaluated for multiple indications simultaneously. This approach reduces the time risk and the possibility of imminent intellectual property expiration, which otherwise requires the reinvestment of significant resources to force the profiling of the same molecule [24]. Repurposing a drug requires a comprehensive understanding of the biological and molecular pathways that a drug can modulate, as well as its interaction with endogenous biomolecules. With a comprehensive understanding of the drug and its affected pathways, this hypothetical risk can be completely reduced, resulting in effective repurposing of a drug. [24]

For example, pharmaceutical companies are not sufficiently incentivized to con- tribute to drug research without a guaranteed returnon investment, as in the case of rare cancers such as pediatric cancers (https://www.anticancerfund.org). This challenge hinders thenormal process of drug discovery due to the reluctance to invest on the part of pharmaceutical companies and drug developers (24)

5.2 Challenges and Significance of drug repurposing

N0.	Significance	challenge
1.	Safety ensures	Regulatory requirement lack of knowledge
2.	Time Save and Money	Financial lack
3.	Higher global revenue stream	Clinical trial problem
4.	Out licensing probability	Intellectual property issue
5.	Identify the new uses for old drugs	Market analysis demand

table 2- challenge and significance of drug repurposing

VI. DRUG DATABASE AND CLINICAL OBSERVATION IN DRUG RE- PURPOSING

6.1 Drug Database

Since the development of drug repurposing in the field of drug discovery, many databases (DB) have been created, which include different information. Figure.5 classifies them according to their information content and applications in drug repositioning and describes how each category can be used in drug design and repositioning.

Except database, tools (TO), which are created on the basis of databases and can be used for the reuse of drugs. After explaining his skills and the substance is examined and discussed. Databases (DB), their abbreviations (ABR) used in this article, web links, a brief description of them and their references (REF) are listed in Table 3. Figure 10 shows the databasesand their data content that are classified as such in Figure 5.

For example, the DrugB database integrates enzymes, 3D structures, drug and clinical targets, pathways and side effect data. Additionally, for all databases, their basic category is presented.

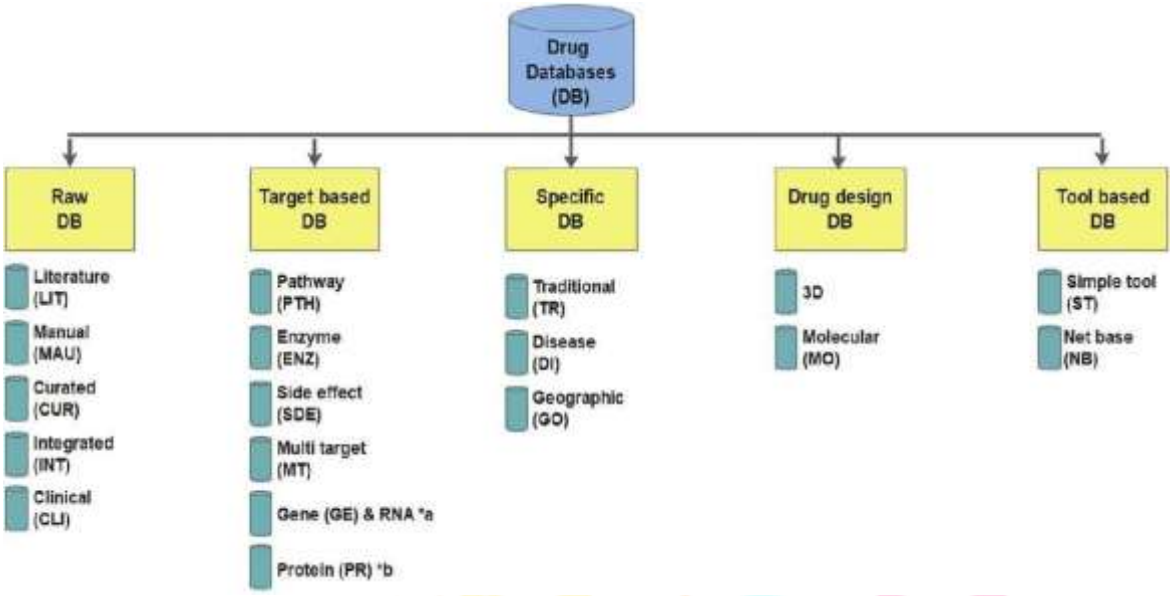

fig 5. a database classification

Group Category databases

Group	DB/TO	Abr.	Weblink	Description	Ref
Raw data category	THIN	THIN	https://www.ucl.ac.uk/	Thin has collected result related todrug & disease	25
Target based category	Drug Bank	Drug B	http://www.drug.bank.ca/	Drug bank provide comprehensive database of drug	26
Special category	Drug Path	DPTH	http://www.cuilab.cn/drugpath	DPTH contains pathways which are induced by drugs	27
Drug design category	CheMBL	CHM	https://www.ebi.ac.uk/chembldb/	CheMBL consists of a large numberof drug-like compounds for drug discovery applications.	28
Tool based category	Drug Net	DNET	http://genome.ugr.es:9000/drug net	DNET integrates heterogeneous data and prioritizes effects of drugson diseases	29

table 3 – the investigated databases

6.2 Clinical Observation

French The official illustration of a retrospective clinical analysis leading to the reuse (or distribution if the drug had otherwise failed for its primary indication) of an investigational patch is sildenafil [30]. Other cases of repurposing opportunities arising from retrospective clinical and/or pharmacological analyses include aspirin in colorectal cancer (the US Preventive Services Task Force published draft recommendations in September 2015 regarding the use of aspirin to help treat cardio- vascular disorders and colorectal cancer [31], raloxifene. in breast cancer (Evista; approved by the FDA to reduce the risk of cancer [32] However, the cases cited below are not the result of a methodical analysis of clinical data. can be obtained from a variety of sources, including DMPs,post-marketing surveillance data, and clinical trial data contain a large amount of data on patient problems, both structured and unstructured.

French Individual and pathophysiological data, including the results of laboratory tests and drug determination data, are more structured; however, EHRs also contain a significant amount of unstructured information, such as clinical descriptions of patients' symptoms and signs (which are important in determining the disease phenotype) and data from the image. This wealth of data present in the EHR can be used as a source of link signals for the reuse of drugs11; In addition, the large amount of data from EHR also provides high statistical power [33]. Paik and colleagues [34] extracted clinical signatures from more than 13 times the EHR of a tertiary care facility, including >9.4 million laboratory tests in half a million cases, in addition to various genomic signatures for identify more than 17,000 known drug-disease associations; This approach led to the identification of the anti-asthmatic terbutaline sulfate as a promising agent for the treatment of multiple sclerosis (ALS). UK French Clinical Practice

Research Datalink (CPRD), the Medicines and Healthcare products Regulatory Agency (MHRA) non-hero card system, EudraVigilance (a European suspect reporting database adverse medicinal reactions managed by the European Medicines Agency EMA), the FDA Ad- verse. The World Health Organization (WHO) Event Reporting System (FAERS) and Global Database of Adverse Drug Reactions (VigiBase) contain valuable data for cases, diseases and medications that can serve as important resources for drug reuse analysis.

However, major challenges remain in the penetration and utilization of EHR data, including ethical and legal barriers that limitaccess to data and the difficulty of eradicating information previously present in these databases. Building additional search capabilities into EHR databases can help improve their utility for various downstream openings similar to drug repurposing.
Natural language processing and machine learning methods can also be valuable. Post- marketing surveillance data and clinical trial data are two other important sources of big data, but access may be restricted for marketing or privacy reasons. However, there is an increase in consumption that indicates that opening access to a similar wealth of information can support the exploration of drug development. In October 2016, the EMA began providing direct public access to clinical trial data submitted by pharmaceutical companies and has published reports on six different medicines to date (European Medicines Agency ClinicalData; see affiliate links).

VII. ARTIFICIAL INTELLIGENCE IN DRUG REPURPOSING

With the advancement of computational artificial intelligence, the obstacles and limitations of a computational approach to drug repurposing can also be infinitely reduced. Artificial intelligence (AI) can be essentially characterized as the limitation of human intelligence exemplified by machines that incorporate reasoning, organization, learning, and cognition to enhance the probabilitiesof achieving distinctive goals under extraordinary load and emergency conditions, such as pandemics or diseases of unknown etiology. The rise of AI is inevitable, especially in the increasingly complex management of drug discovery and repurposing.
With an ever-expanding body of chemical and natural data, the need for efficient computational data mining algorithms isessential to ensure a fast, highly efficient, and inexpensive drug discovery process [35].

While AI is part of computer-aided design (CADD), this computational approach has been used for decades for drug discovery and repositioning. Machine Learning (ML) suggestions, such as logistic regression (LR), faithful Bayesian classifier (NB), calculation of k-nearest neighbors (KNN), machine learning regression (MLR), Gaussian scheme and others tools, are supported. on the integration of AI for the intended translation of drug repositioning openings [36]. Today, the suggestion of ML, accompanied by the development of AI, has evolved into deep learning (DL) models, which promote the formation of more grounded information, accompanied by proven results in the shortest possible time and with high efficiency. In this case, with theuse of deep neural network (DNN), Ma and his colleagues have successfully overcome many obstacles. In comparison, the difficulties encountered in the preparation and screening of many compounds have been associated with the improved prediction accuracy of the quantitative structure-activity relationship (TSAR) framework, which is essential for predicting target and off- target activity. target in quiescent detection [37]. That said, drug-target interaction (DTI) recognition evidence is a fundamental perspective to consider in drug repositioning. DTI in drug repositioning is found in traditional ligand- and structure-based models,which use TSAR to read the normal conditioning of target particles with the assumption of virtually identical atoms that allow virtually identical natural packing and certified mimics of atomic bond [36]. However, the limitations of these common computational models draw attention to DL models. In this case, a computational system based on DL, Deeds, effectively predicted the unused Otis among approved drugs and targets directly without the need to isolate the targets into different classes. The works have also been shown to outperform other ML models, such as Subjective Forest [37] and Support Vector Machine (SVM). This approach offers great potential to help exploit unexploited sedative targets based on expectations as targets, or untapped targets that treat drugs [36]

fig.6 drug discovery with the help of AI

VIII. ADVANTAGES OF DRUG REPURPOSING

Drug repurposing is a new way of finding new uses outside the scope of the original medical indication for existing drugs. Otherterms widely used in this context are drug repositioning, drug reprofiling, or drug repurposing, which are all slightly different in meaning, but are widely used synonymously with drug repurposing. Drug repurposing offers a number of advantages over conventional drug discovery and development, as shown below and in Figure.7[38]

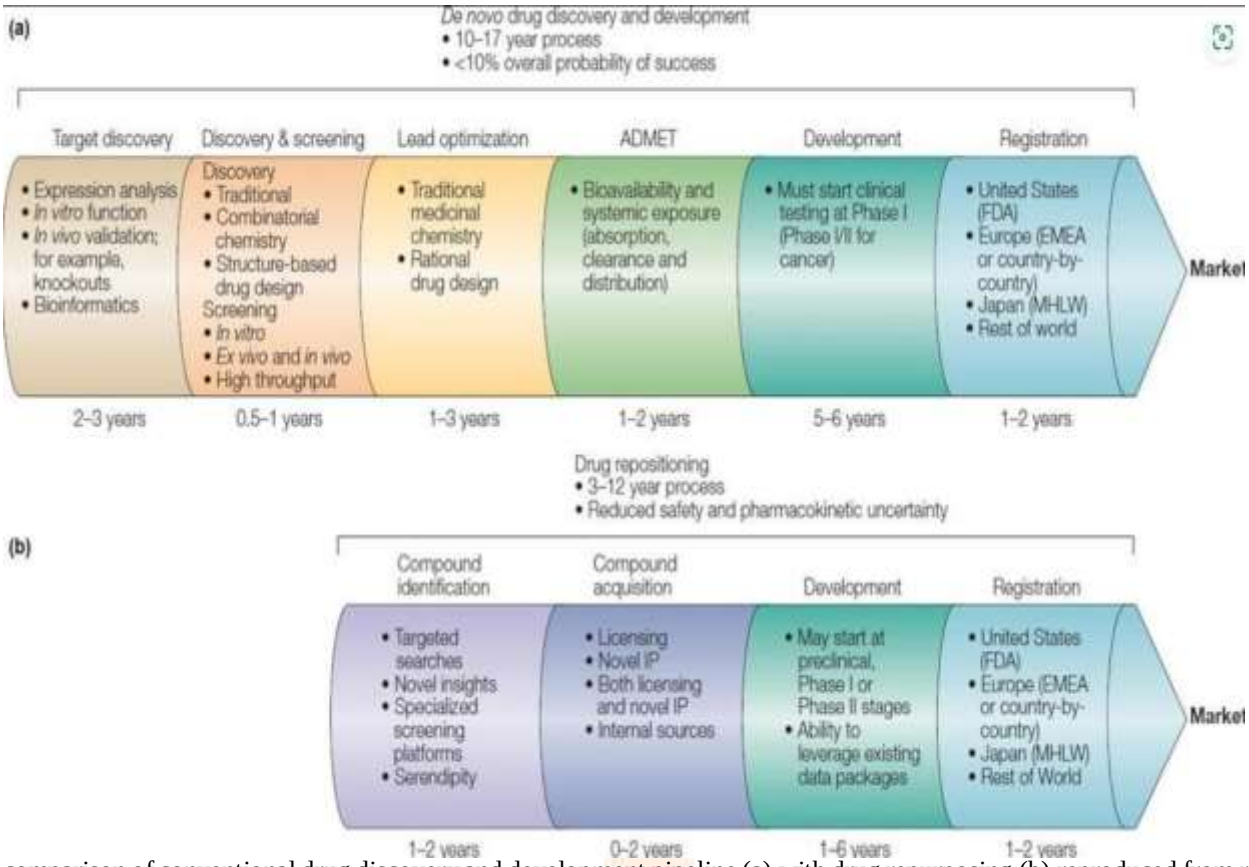

fig 7. comparison of conventional drug discovery and development pipeline (a) with drug repurposing (b).reproduced from ref. [38] with permission from springer nature, copyright 2004.

a) Faster development time

Drug development periods are much shorter compared to the conventional system due to the lack of preclinical, safetyand tolerability data.

b) Reduced cost

Since most of the preclinical and phase I/II work has already been done, repurposing a drug for a new indication willresult in significant cost savings.

c) Faster regulatory approval

Since a repurposed drug already has positive preclinical and safety data, unsupervised approval will be easier and fasterto obtain

d) A better understanding of disease mechanisms

A repurposed drug can uncover new targets, pathways and previously unknown biomarkers in a disease. This will allow further exploration of disease mechanisms and may lead to the development of new molecules that are structurally analog-gous, but more potent than the targeted drug

e) Save time and money

Saving time and money The current expensive and time-consuming drug discovery paradigm has limited the broadergrowth of drug development. With the significant costs, the high threat and the slow pace of drug discovery, a very necessary approach is important and necessary to quickly start the development of drugs to meet the demand

f) Bioinformatics databases available for drug candidates

Drug repositioning opens up great opportunities, in which Researchers can identify existing drugs that recognize specific targets based on previously discovered, without the need for large-scale experiments. This is

achievable thanks to the continuous expansion of bioinformatics and chemoinformatic databases such as proteomics databases (UniProt), genomic databases (Entrez-Gene), and pharmaceutical databases (DrugBank/Drug Central/PubChem), which provide vital gene expression and chemical structures against which important candidates can be screened for drug repositioning

IX. FUTURE PERSPECTIVE IN DRUG REPURPOSING

Human diseases are transmitted by complex underlying components that can develop or be acquired from many sources, such asgenetic abnormalities, infectious diseases, degenerative diseases and more. Diseases often involve multiple cascades of complexcellular pathways, which may differ in some people. In different human populations, each person has a unique set of acquired ornon-inherited genetic abnormalities that may cause some people to respond less or not at all to medications or generic drugs.
Confirmed medications can be invalid for a particular person if they are deficient in a specific drug target and cannot respond in ausual way to a specific medication.

This situation implies the need for personalized medication to adapt to each individual procedure, since drug efficacy can produce significantly different qualitative profiles due to the heterogeneity of human infection [39]. To reduce the need for sedative sufficiency, drug repositioning plays an imperative role. With the advancement of next-generation sequencing innovations, personalized genomic studies can be performed with a positive approach. This can lead to the best drug with high efficacy at the lowest possible levels of harm to the individual, unlike routine treatment that aims for the maximum tolerated dose [40].

X. CONCLUSION

Drug recovery has become a powerful tool in modern drug development, providing a sustainable path to address unmet medical needs, particularly in areas where new drug discovery has proven difficult. Although there are many obstacles, including intellectual property limitations, limited regulatory frameworks, and the need for deeper biological understanding, the integration of computational techniques and big data analysis offers promising paths to overcome these problems Enhanced collaboration between industry, academia, and regulators will be essential to advance reuse efforts. Moving forward, it will be essential to refine data integration methods, improve predictive algorithms, and develop clear regulatory guidelines to fully realize the potential of drug repurposing. By addressing these challenges, the scientific and medical communities will be able to capitalize onexisting pharmacological knowledge, thereby accelerating the availability of new therapies and improving patient outcomes.

REFERENCES

1.Pushpakom S et al. Drug repurposing: progress, challenges and recommendations. Nat Rev Drug Discovery 2019;18:41–58.

2.U.S.Department of Health and Human Services. The drug development process. Available at: https://www.fda.gov/ForPatients/Approvals/Drugs/default.htm.

3. Aube´,J.(2012)Drugrepurposingandthemedicinalchemist.ACSMed.Chem.Lett.3,4 42–444

4. Sertkaya A. Examination of clinical trial costs and barriers for drug development. Washington, DC: US Department ofHealth and Human Services, Office of the Assistant Secretary for Planning and Evaluation; 2014.

5. Yeu Y, Yoon Y, Park S. Protein localization vector propagation: a method for im- proving the accuracy of drugrepositioning. Mol Bio syst. 2015;11(7):2096–2102.

6. Zhou Y, Wang F, Tang J, Nussinov R, Cheng F. Artificial intelligence in COVID- 19 drug repurposing. Lancet DigitHealth. 2020;2(12):e667–676.

7. Zhou Y, Hou Y, Shen J, Mehra R, Kallianpur A, Culver DA. A network medicine approach to investigation and population-based validation of disease manifestations and drug repurposing for COVID-19. PLoS biology. 2020;18(11):3000970.

8. Cheng F, Desai RJ, Handy DE, Wang R, Schneeweiss S, Barabási A-L, et al. Net- work-based approach to predictionand population-based validation of in silico drug repurposing. Nat Commun. 2018;9(1):1–12.

9. Zhou Y, Hou Y, Shen J, Huang Y, Martin W, Cheng F. Network-based drug repurposing for novel coronavirus 2019-nCoV/SARS-CoV-2. Cell Discovery. 2020;6(1):14.

10. Cheng F. In silico oncology drug repositioning and poly pharmacology. Methods Mol Biol. 2019;1878:243–61. 11.S.Dotolo, A. Marabotti,

A. Facchiano, R. Tagliaferri, A review on drug repurposing applicable to COVID-19, Briefings

in Bioinformatics. 22 (2021) 726–741.

12.N.T. Issa, J. Kruger, S.W. Byers, S. Dakshanamurthy, Drug repurposing a reality: from computers to the clinic, ExpertReview of Clinical Pharmacology. 6 (2)(20 13) 95–97.

13.Q. Vanhaelen (Ed.), Computational Methods for Drug Repurposing, Springer, New York, 2019.

14. Ashburn TT, Thor KB (2004) Drug repositioning: identifying and developing new uses for existing drugs. Nat Rev Drug Discov 3(8):673–683

15. Vaidya, B. et al. (2019) Cyclodextrin modified erlotinib loaded PLGA nano particles for improved therapeutic efficacy against non-small cell lung cancer. Int. J.Biol.Macromol. 122, 338–347

16. Pushpakom S. et al., Drug repurposing: progress, challenges and recommendations, Nat. Rev. Drug Discovery, 2019,vol. 18 (pg. 41-58)

17. Pembrolizumab, ipilimumab, and aspirin in treating patients with melanoma that is metastatic or cannot be removedby surgery NCT03396952. Available at: https://www.cancer.gov/about-cancer/treatment/clinical-trials/search/v**?** id=NCI-2017-02441.

18.9 old drugs that learned new tricks: the head of the National Institutes of Health Available at: https://blog.ted.com/9-old-drugs-that-learned-new-tricks-the-head-of-the-national-institutesofhealth-shares-medicines-that-turned-out-to- have-multiple-uses/

19. Celgene. Celgene Reports Fourth Quarter and Full-Year 2016 Operating and Fi-http://www.celgene.com/press_release/celgene-reports-fourth-quarter-and-full-year-2016-operating-and-financial- results/

20. Lenz W. Thalidomide and congenital abnormalities, Lancet, 1962, vol. 1 pg. 45

21. Sleigh, S.; Barton, C. Repurposing Strategies for Therapeutics. Pharm. Med.2010, 24, 151–159.

22. Gns HS, Gr S, Murahari M, et al. An update on Drug Repurposing: Rewrittensaga of the drugs fate. Biomed Pharma-cother 2019; 110:700–16., Lippmann C,Kringel D, Ultsch A, et al. Computational functional genomics-based approaches in analgesic drug discovery and repurposing. Pharmacogenomics 2018; 19:783–97.,Xue H, Li J, Xie H, et al. Review of drug repositioning approaches and resources.Int J Biol Sci 2018; 14:1232–44.

23. Pahud, D. et al. (2014) A new market access path for repurposed drugs. Avail-able at:2014 In:https://www.kauffman.org/what-we-do/research/2014/05/a-new-

24. Novac, N. (2013) Challenges and opportunities of drug repositioning. Trend-sPharmacol. Sci. 34, 267–272

25. J.D. Lewis, R. Schinnar, W.B. Bilker, X. Wang, B.L. Strom, Validation studies of the health improvement network(THIN) database for pharmacoepidemiology research,Pharmacoepidemiol. Drug Saf. 16 (2007) 393–401.

26.H. Zeng, C. Qiu, Q. Cui, Drug-Path: A Database for Drug-Induced Pathways,Database, 2015, (2015).

27. J.D. Lewis, R. Schinnar, W.B. Bilker, X. Wang, B.L. Strom, Validation studies of the health improvement network(THIN) database for pharmacoepidemiology research,Pharmacoepidemiol. Drug Saf. 16 (2007) 393–401..

28. A. Gaulton, L.J. Bellis, A.P. Bento, J. Chambers, M. Davies, A. Hersey, Y. Light, S. McGlinchey, D. Michalovich, B. Al-Lazikani, ChEMBL: a large-scale bioactivity database for drug discovery, Nucleic Acids Res. 40 (2011) D1100–D1107.

29. V. Martínez, C. Navarro, C. Cano, W. Fajardo, A. Blanco, DrugNet: network-based drug disease prioritization byintegrating heterogeneous data, Artif. Intell. Med. 63(2015) 41–49.

30.Ashburn, T. T. & Thor, K. B. Drug repositioning: identifying and developing new uses for existing drugs. Nat. Rev.Drug Discov. 3, 673–683 (2004).

31.US Preventive Services Task Force. Final recommendation statement. Aspirin use to prevent cardiovascular diseaseand colorectal cancer: preventive medication.USPreventiveServicesTaskForcehttps://www.uspreventiveservicestask-force.org/Page/Document/RecommendationStatementFinal/aspirin-to-prevent-car-diovascular-disease-and-cancer (2017).

32.Cavalla, D. & Singal, C. Retrospective clinical analysis for drug rescue: for new indications or stratified patient groups. Drug Discov. Today 17, 104–109(2012). Jensen, P. B., Jensen, L. J. & Brunak, S. Mining electronic health records: towards better research applications and clinical care. Nat. Rev. Genet. 13, 395–405(2012).

33.Paik, H. et al. Repurpose terbutaline sulfate for amyotrophic lateral scleros isusing electronic medical records. Sci. Rep. 5, 8580 (2015).

34.Huang, Y. H. & Vakoc, C. R. A. Biomarker harvest from one thousand cancercell lines. Cell 166, 536–537 (2016).

35.Wang, L.; Ding, J.; Pan, L.; Cao, D.; Jiang, H.; Ding, X. Artificial intelligence facilitates drug design in the bigdata era. Chemom. Intell. Lab. Syst. 2019, 194,103850.

36.Napolitano, F.; Zhao, Y.; Moreira, V.; Tagliaferri, R.; Kere, J.; D'Amato, M.;Greco, D. Drug repositioning :A machine-learning approach through data integration. J. Cheminform. 2013, 5.

37.Vanhaelen, Q.; Mamoshina, P.; Aliper, A.; Artemov, A.; Lezhnina, K.; Ozerov,I.; Labat, I.; Zhavoronkov, A.Designof efficient computational workflows for insilico drug repurposing. Drug Discov. Today 2017, 22,210–222.

38.Ashburn T. T., Thor K. B.Drug repositioning: identifying and developing new uses for existing drugs, Nat. Rev. DrugDiscovery, 2004, vol. 3 (pg. 673-683)

39.Amir-Aslani, A.; Mangematin, V. The future of drug discovery and development: Shifting emphasis towards personalised medicine. Technol. Forecast. Soc.Chang. 2010, 77, 203–217.

40.Janku, F.; Stewart, D.; Kurzrock, R. Targeted therapy in non-small-cell lung cancer—Is it becoming a reality?Nat. Rev. Clin. Oncol. 2010, 7, 401–414.