



A Review on: Drug Repurposing

¹Dr Gajanan Sanap, ²Uttara Joshi, ³Vinita Pol

¹principal, ²Assistanat Proffesor , ³student

Abstract:

The drug development is a very time consuming and complex process.

Drug development process is Expensive, success rate for the new drug development is very small and in recent year, decrease the new drug development; Hence we are using the drug by Repurposed process. and this process has become a popular strategy in recent year. Drug repurposing involves the identification of new applications for existing drugs at a lower cost and a shorter time. The drug Repurposing as an approach finds new therapeutic uses for current candidates or approved drugs, different from its original application. The main aimed of drug repurposing is to reduce costs and research time investments in research and development. Already approved medicines – and many discarded compounds have been tested in human so comprehensive information exists on their pharmacology, dose and formulations.

Drug repurposing plays important role, because it helps to preclinical development. it reducing time efforts, expenses and failures in drug discovery process. it is also called as drug repositioning, drug redirecting , drug reprofiling.

Advantages of repurposing existing drugs-time and cost to develop a new indication for an existing drug may be significantly less compared to developing a new drug from scratch because –most of the nonclinical drug development has already been done inducing chemistry, manufacturing and control, animal toxicity and clinical pharmacology there is clinical data on safety in a population that may be relevant to the novel use.

Keywords: Drug repurposing, examples of different Repurposing drugs and their targeted actions, Need of drug repurposing.

Introduction:

Drug repurposing (DR) is also known as drug repositioning, drug re-tasking, drug reprofiling, drug resuming, drug recycling, drug redirection, and therapeutic switching. It can be defined as a process of identification of new pharmacological indications from old/existing/failed/investigational/already marketed/FDA approved drugs/pro-drugs, and the application of the newly developed drugs to the treatment of diseases other than the drug's original/intended therapeutic uses.[1-3]

The novel drug development is a time-consuming and complex process in which investment rate is high and success rate being small. In recent years, decrease the new drug development or approved for the clinical use. Then the Drug repurposing is a powerful tool used to support the novel drug discovery process. In the process finding the new uses of banned drugs from market.

In drug repurposing process –if a mechanism of a drug is known that time finding new indications. i.e., if one molecule acts on the same target and they produce two dissimilar therapeutic actions. (on targeted repurposing).

In repositioning the unknown pharmacological mechanism for finding the new therapeutic indications, Drug's act on another new targets, other than its actual use (off target repurposing). [5,28,29.]

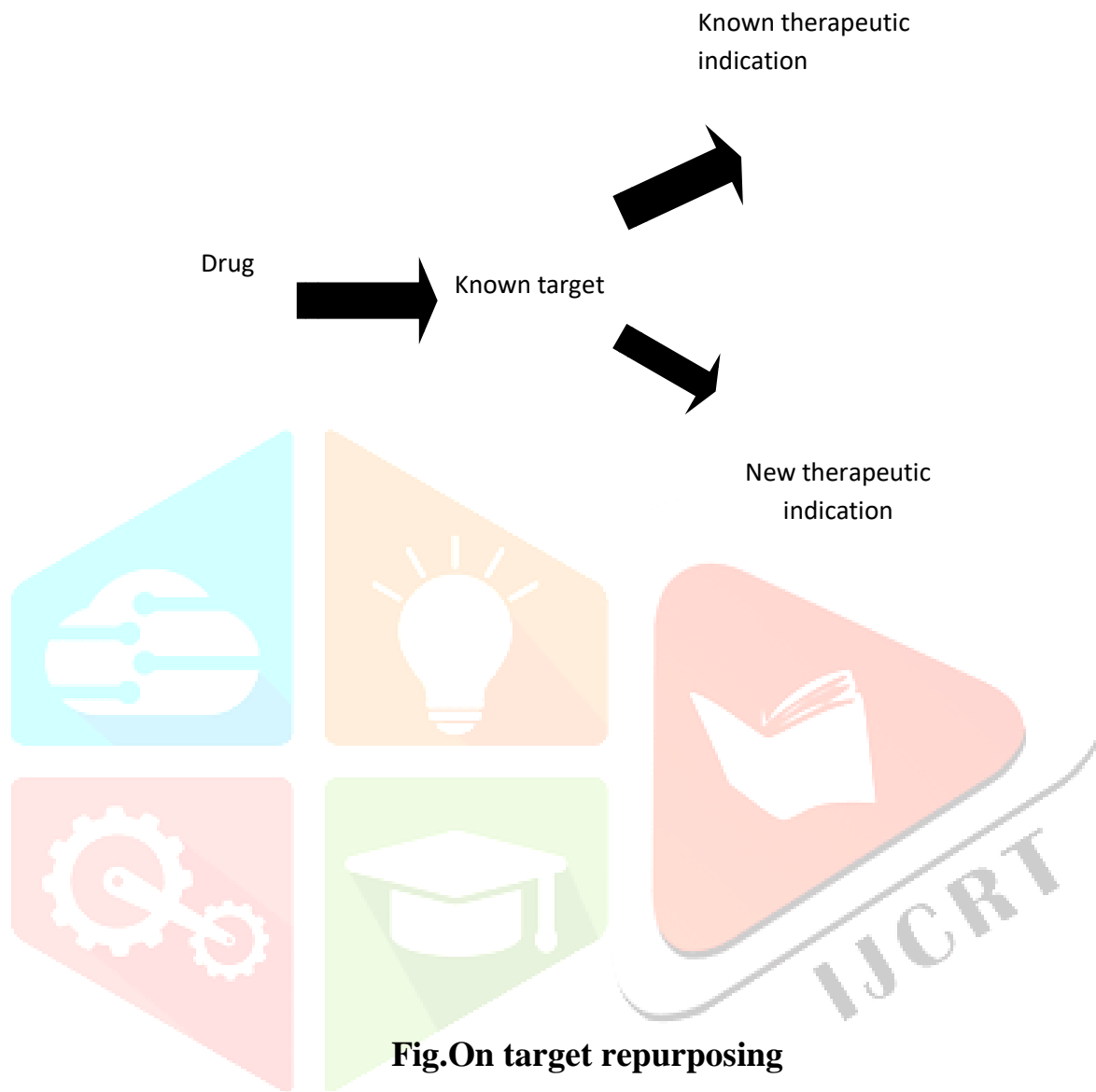


Fig.On target repurposing

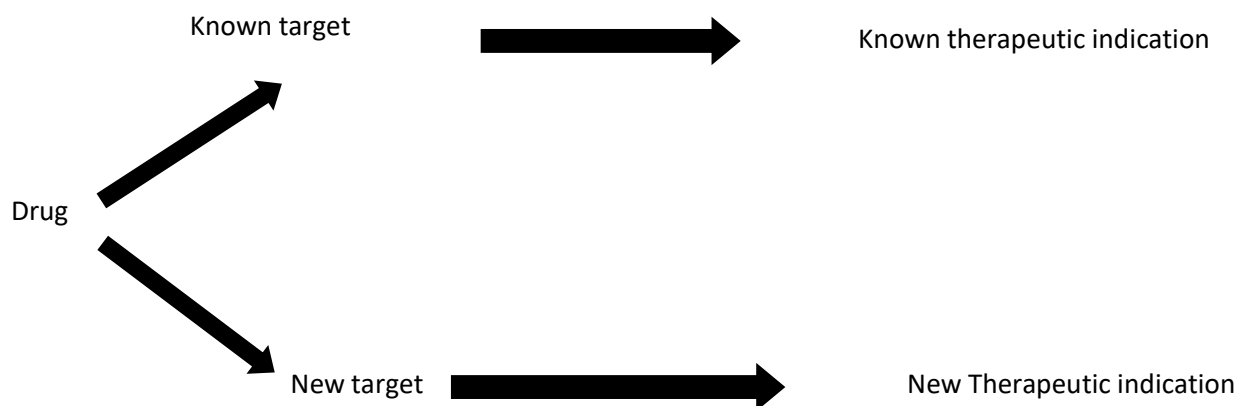
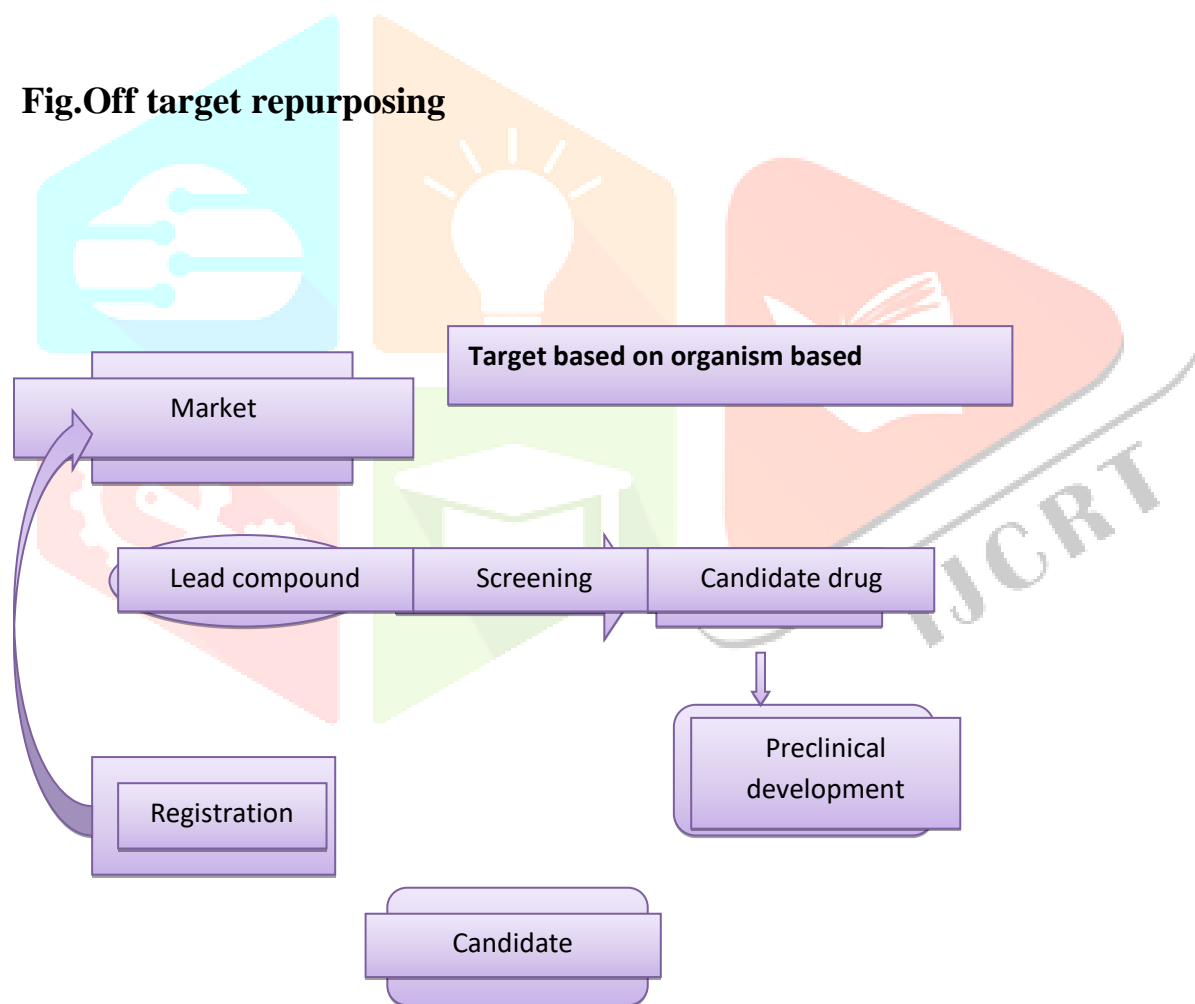
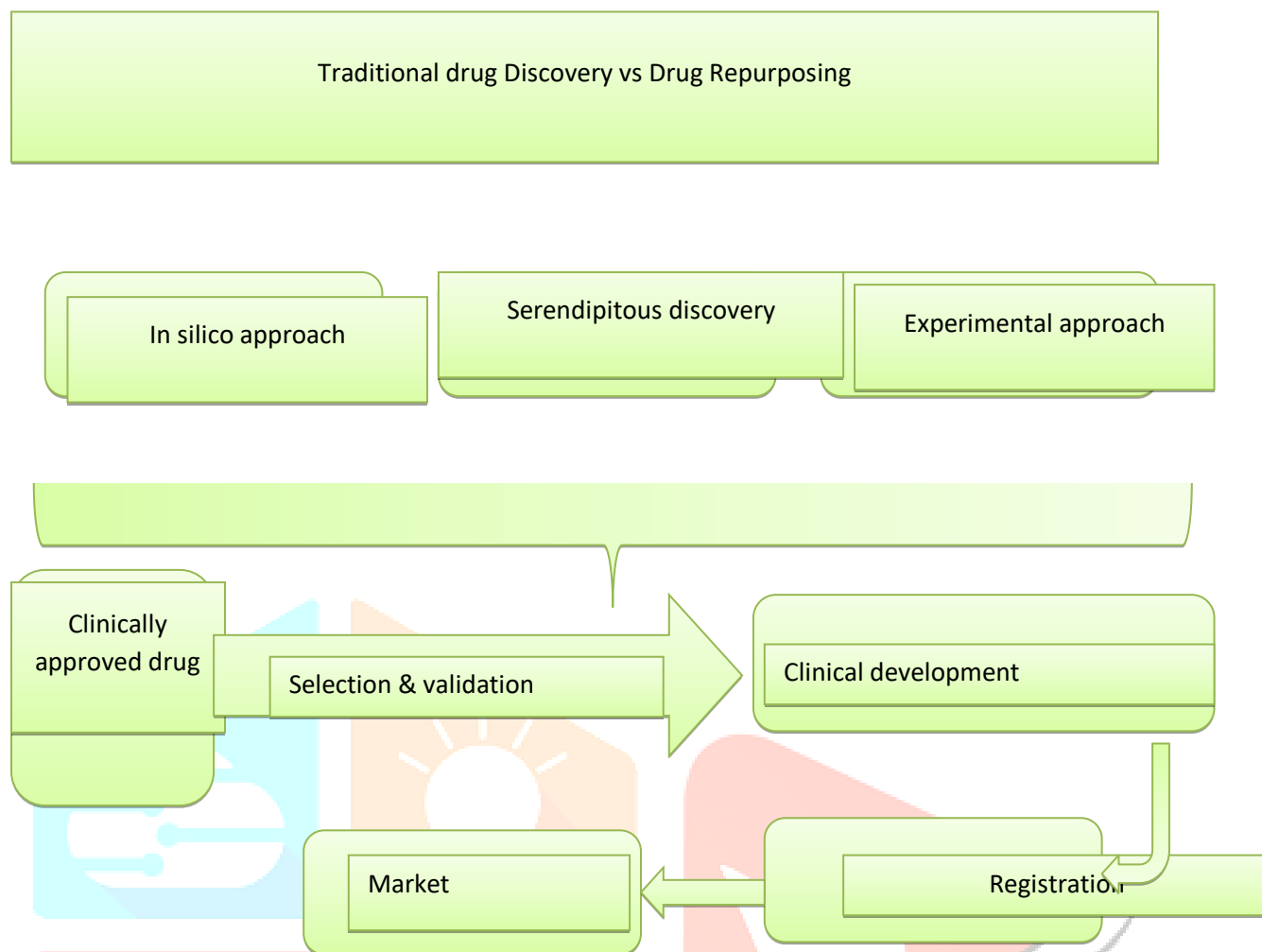


Fig. Off target repurposing





Charts of drug repurposing compared to traditional drug development [52.53].

Traditional drug discovery is time consuming, costly and risky process.owing to the large investment, excessive attrition & declined output,drug repurposing has become a blooming approach for the identification & development of new therapeutic.The some process that results in drug repurposing can also be used for the predication of adverse events of known or novel drugs.Drug repurposing holds the potential to bring medication with known safety profile to new patient population.A variety of innovative computational methods to enable systemic repurposing screens, experimental as well as through in silicon approaches,have emerged.Drug Repurposing has become one of the most active areas in pharmacology since the last decade.compared to traditional drug development,drug repurposing may provide more systemic & significantly less expensive approaches in discovering new treatments for complex disease.

Network medicine for disease module identification and drug repurposing with the NeDRex platform is highly active field of research, which has been boosted even further with the advent of the recent COVID-19 pandemic. NeDRex allows researchers from pharmacology & biomedicine to leverage their expert knowledge for discovering drug repurposing candidates via state-of-the-art network medicine method

[8-10]

- Drug repositioning has several advantages in comparison with traditional approaches to drug discovery program, a significant reduction of the time spent in R and D can be

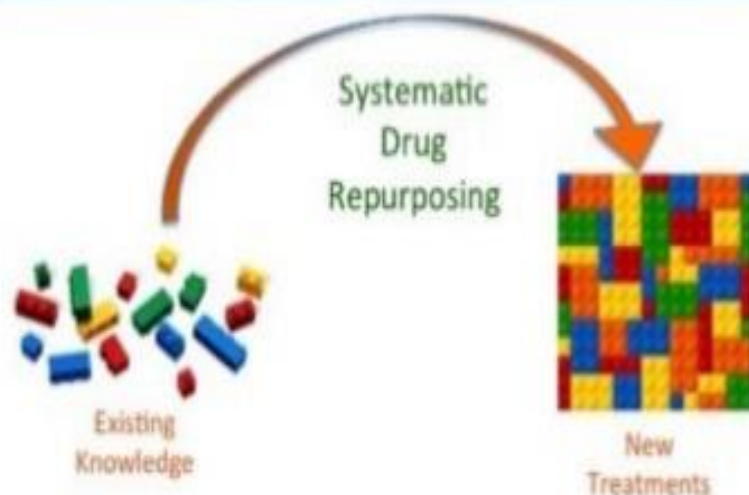
Observed. It is estimated that 10-16 years are spent for the development of a new drug, while in DR the estimated time is between approximately 3 to 12 years. [15-17]

Drug repurposing by connecting drug targets with disease..

i.e., "one disease –one target-one drug" this is how we traditionally think about pharmaceutical drugs, but many of them are actually effective for more than one disease.

Now a research team has used novel big data analytics methods to trawl through massive pharmaceutical data, looking for drugs having a high potential to be what the scientists call "repurposable". Exemplified by sildenafil and thalidomide, is a promising way to explore alternative indications for existing drugs. Recent research has shown that bioinformatics-based approaches have the potential to offer systematic insights into the complex relationships among drugs, targets and diseases necessary for successful repurposing.

Drug repurposing



➤ Examples of different current status of repurposed drugs :[22-28]

Drug Name	Category	Action	Repurpose	Pharmacological action of the drug in DR process
Favipiravir	Antiviral	Viral infection	Covid-19	Undergoes phosphorylation to favipiravir-RTP, which is the active form of this drug. It exerts its antiviral effect.
Remdesivir	Antiviral	Viral infection	Anticoronavirus agent	Remdesivir blocks a particular enzyme that is required for viral replication

Rosiglitazone	Thiazolidinedione class	Anti diabetic	Malaria as an adjunct therapy	Agonist of peroxisome proliferators activated receptor gamma (PPARA)
Aspirin	Analgesic and antipyretic	Pain killer	Thrombosis	Its effect on homeostasis is to impair platelet aggregation via inhibition of platelet thromboxane A2 synthesis.
Sildenafil	Phosphodiesterase inhibitor	Erectile dysfunction	Angina pectoris	Reduced systemic & pulmonary arterial pressure & cardiac output
Amphotericin B	Antifungal	Fungal infection	Leishmaniasis	Binding to parasite ergosterol precursors & loss of the permeability
Amantadine	Anti Viral	Influenza	PD	Inhibit the reuptake of dopamine & noradrenalin

Bupropin SSRI	Antidepressant	Depression	Smoking cessation	Action through dopamine & noradrenaline
Cimetidine	Antacid (Antihistamine)	Gastric ulcer	Breast, lung, & prostate cancer	Inhibition of cancer cell proliferation
Favipiravir	Antiviral	Influenza	Covid -19	Favipiravir RTP binds to and inhibits RNA- dependent polymerase
Lopinavir/Ri tonavir	Antiretroviral	HIV/AIDS	Covid-19	As Lopv is a Protease inhibitor, inhibi t, the action of 3 cl pro.
Ivermectin	Antiretroviral	Scabies, helminth iasis	Covid-19	Acts by inhibiting the host importin alpha /beta -1 nuclear transport protein
Tocilizumab , IL-6 inhibitor	Immunosuppressi ve	RA	Covid-19	Bind to both IL-6R & SIG- 6R & inhibit classical & trans-sign

Material and methods-DR is like it takes existing drugs already approved for human use, and identifies new illness that they could treat.

The methodologies included in DR process are divided into three classes are:

1. Drug oriented
2. Target oriented
3. Disease/therapy oriented

1. Drug oriented: In drug oriented mechanism the structural characteristics, adverse effects, side effects & phenotypic screening of the drug molecules is evaluated. This strategy is meant for identifying molecules with biological effects based on cell/animal assay. This type of repositioning methodology is based on traditional pharmacology & drug discovery principles, significant success in DR have been achieved with this oriented profile, such as discoveries with sildenafil. The new uses of drug discovered randomly, especially during the clinical Research & development trials. [31-33]

2. Target oriented: In the target oriented the in vitro and in vivo high-throughput the high-content screening of molecules. In target oriented drug side effects or find their new uses. Then they are mainly target on site & shows their effects. Target-based methods discover drug based upon known target molecules. [35-37]

3. Disease /therapy oriented: In drug repurposing any disease or treatment if there is more diseases or information available. Therefore the proper information with possible are adding of their mechanisms, adverse effects & side effects. In the case, drug repurposing and be guided by the disease and treatment based upon availability of given information. [5,23]. The current success in drug repurposing has primary results of observed useful of repurposing. Repurposing drugs requires finding novel therapeutic indications compared to the ones for which they were already approved. This is an increasingly utilized strategy for finding novel medicines, one that capitalizes on previous investments while derisking clinical activities. This approach is of interest primarily because we continue to face significant gaps in the drug–target interactions matrix and to accumulate safety and efficacy data

during clinical studies. Collecting and making publicly available as much data as possible on the target profile of drugs offer opportunities for drug repurposing, but may limit the commercial applications by patent applications. Certain clinical applications may be more feasible for repurposing than others because of marked differences in side effect tolerance. Other factors that ought to be considered when assessing drug repurposing opportunities include relevance to the disease in question and the intellectual property landscape. These activities go far beyond the identification of new targets for old drugs



Fig. Drug Repositioning

•Discussion & conclusion: In this review conclude that the knowledge about Drug Repurposing.

Drug repurposing is a field of drug research whose importance has been increasing in the recently situation, due to several advantages, such as the possibility to shorten the clinical trials, the extension of the life of an old drug by finding a new therapeutic effect.

The urgency to find drugs to face the different types of diseases in the pandemic has tremendously pushed this kind of research in the past months. As drug repositioning approach offers significant reduction in R & D costs, greater chances of success, shorter research time & lower investment risk, it has gained increasing market demands. Because these advantages are beneficial for discovery scientists, drug researchers, consumer and pharmaceutical

companies , enabling the application of novel approaches of repurposing strategy in the drug discovery program for almost all human disease.almost 30% in india using the re-purposing the existing drug.we notice that in Repurposing the common feature of these studies.A proverb says: "haste makes waste". In the era of precision medicine ,the drug Repurposing strategy has become very much useful to establish the unknown mechanism of action of drugs through exploration of novel disease/signalling pathways or off-targets & target specific mechanism. However,the drug repurposing can be successfully utilized in the discovery and development of new drugs with novel and effective therapeutic indication for human diseases.

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Hema Sree GNSa

, Saraswathy GRa,a

, Manikanta Muraharia,c

, Mamatha Krishnamurthya,b

a "Pharmacological Modelling and Simulation Centre", M.S.Ramaiah University of Applied Sciences, Bangalore, Karnataka, India.

b Department of Pharmacy Practice, Faculty of Pharmacy, M.S.Ramaiah University of Applied Sciences, Bangalore, Karnataka, India.

c Department of Pharmaceutical Chemistry, Faculty of Pharmacy, M.S.Ramaiah University of Applied Sciences, Bangalore, Karnataka, India.

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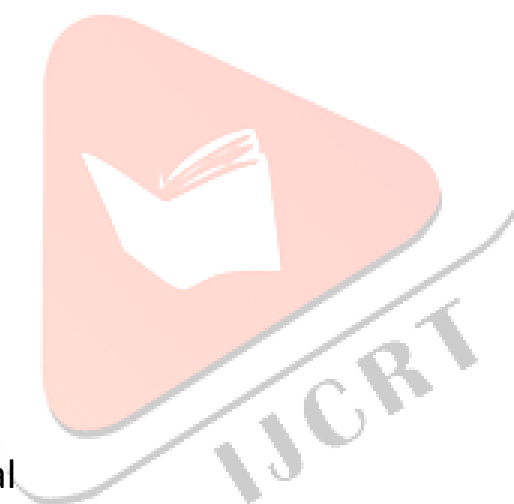
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