ISSN: 2581-5989
PubMed - National Library of Medicine - ID: 101738774

International Journal of Dental Science and Innovative Research (IJDSIR)
IJDSIR : Dental Publication Service
Available Online at: www.ijdsir.com
Volume – 7, Issue – 2, March – 2024, Page No. : 126 - 131

Repurposing Drugs in Dentistry - The Future Wield

[1]R Vaishali Kamak, MDS, Department of Periodontics, Meenakshi Ammal Dental College and Hospital, Chennai, Tamilnadu.

[2]Geetha A, Professor and Guide, Department of Periodontics, Meenakshi Ammal Dental College and Hospital, Chennai, Tamilnadu.

[3]Prashanthi, Assistant Professor, Department of Periodontics, Meenakshi Ammal Dental College and Hospital, Chennai, Tamilnadu.

[4]Jaideep Mahendra, Professor and Head, Department of Periodontics, Meenakshi Ammal Dental College and Hospital, Chennai, Tamilnadu.

Corresponding Author: R Vaishali Kamak, MDS, Department of Periodontics, Meenakshi Ammal Dental College and Hospital, Chennai, Tamilnadu.

Citation of this Article: R Vaishali Kamak, Geetha A, Prashanthi, Jaideep Mahendra, "Repurposing Drugs in Dentistry - The Future Wield", IJDSIR- March – 2024, Volume –7, Issue - 2, P. No. 126 – 131.

Type of Publication: Original Research Article

Conflicts of Interest: Nil

Abstract

Worldwide interest in drug repurposing, which discovers novel therapeutic uses for formerly used pharmaceuticals, is a relatively new and recent development. It does so without requiring the substantial financial and time outlay often required for the discovery of new drugs today. Recent research in the realm of dentistry on drug repurposing focuses on achieving dentin regeneration or reducing bone resorption linked to apical periodontitis. Companies use this repurposing tactic to boost productivity by shortening the timelines for drug discovery and development, eschewing some of the priciest drug research techniques.

Keywords: FDA, Drug, Dentin

Introduction

Drug repurposing can also be labelled as drug reprofiling, drug repositioning or re-tasking or therapeutic switching. It focuses on the discovery of novel pharmacological indications for current, failed, old, under exploratory, previously marketed, and FDA-approved medications as well as its use to treat illnesses other than the drug's intended therapeutic purpose. Drug repurposing reduces the traditional drug discovery process's exorbitant costs, high failure risk, and protracted development time.[1]

Need for drug repurposing….?

It has the potential to offer more cost-effective treatment options, medications with favourable side effect profiles, and medications to treat diseases where the currently

available drugs have unfavourable side effect profiles.[2]From an industrial standpoint, drug repurposing is said to be less expensive, less time-consuming, less risky, and more likely to succeed. It can also have a significant impact on the creation of customised medication. Drug repurposing is a very effective method when compared to the conventional medication development process. The difficulties in developing new drugs include rising Research & Development (R&D) expenses, a lengthy drug development timetable, a poor success rate, and regulatory barriers.The therapeutic value of a medicine is maximised, which thus raises the success rate. [3]

Drug repurposing strategies

Drug repurposing frequently operates on three different types of methodologies: biological experimental approaches, computational approaches and mixed approaches. Drug repurposing techniques may be generally divided into activity-based and in silico techniques. High-throughput screening techniques using the medicine or chemical of interest are examples of activity-based approaches that may be applied in vivo (in living creatures) and in vitro identification of compounds with target-specific activity is aided by the hit discovery and confirmation phase.A hit is a compound which has the desired activity in a compound screen. Hits are discovered systematically from data acquired from multiple databases using in-silico, computational, or virtual screening procedures, which also incorporate tools to find drug-target interactions. Even though they require more time and labour than computational methods, activity-based methods are distinguished by fewer false positive hits and simpler screening hit validation than computational methods.[4]The two primary drug repurposing tactics are on-target and off-target. In an on-target strategy, a drug's known pharmacological action is applied to a new therapeutic indication. Although the diseases are different, the biological target is the same in this case.Off-target repurposing is based on drug promiscuity, or more precisely Poly-pharmacology, which implies that a drug could act on numerous targets, and those secondary targets can be employed for a new indication (for instance, cimetidine, a peptic ulcer drug repurposed for lung cancer). Off-target repurposing is considerably more costly and labour-intensive than on-target strategy, but it is also inventive.[5]

Aspirin

Acetylsalicylic acid (ASA), popularly known as aspirin, was the first medication to be modified.Greek physician Hippocrates wrote about using the salicin-rich bark and leaves of the willow tree to treat fever and discomfort about 400 B.C. Salicylic acid was developed in 1832 as a result of Charles Frederic Gerhardt's salicin experiments. A stable aspirin powder formulation was created in 1897 by the German scientist Felix Hoffmann at Bayer to treat his father's rheumatism. Aspirin powder was first made available by Bayer to doctors in 1899, and it quickly rose to the top of the global pharmaceutical market. Aspirin (ASA) is a non-steroidal anti-inflammatory medicine (NSAID) that has been used extensively for many years. It has the ability to modulate illnesses including cardiovascular disease, cancer, and periodontal disease. Through the inhibition of the enzyme cyclooxygenase-2 (COX-2) activity, the anti-inflammatory effects of ASA are achieved by disrupting the biosynthesis of cyclic prostanoids.

The 'gold standard' methodology for evaluating the use of stem cells for regenerative medicine has been developed using the knowledge gained from the research of bone marrow mesenchymal stem cells (BMMSCs). Alternative stem cell sources must be investigated

because BMMSC harvesting necessitates an invasive procedure. Due to their ability for self-renewal and osteogenic differentiation, human dental pulp stem cells (hDPSCs) have been used in the treatment of periodontal disease and the repair of orofacial bone. A new source of accessible stem cells has emerged since Seo et al.'s 2004 discovery of periodontal ligament stem cells (PDLSCs). The PDLSCs showed self-renewal ability and multipotency features when employed for periodontal treatments and regenerative medicine.[6] Aspirin has been shown to improve bone marrow mesenchymal stem cell (MSC) regeneration; however, it is uncertain how aspirin affects hDPSCs' ability to differentiate into osteogenic cells.[7]

The results of earlier investigations suggested that aspirin had a beneficial effect on lowering human alveolar bone loss and increasing periodontal status, which raised the possibility that it created favourable conditions for the health of the periodontal tissues. It was countered, however, that given the complexity of the pathophysiology of periodontitis, it was doubtful that the clinical improvement reported was only attributable to the NSAIDs' suppression of inflammation. It is conceivable that aspirin may have an advantageous effect on the gene expression of growth factors in dental stem cells, resulting in an improvement in periodontal health.

Metformin

For many years, metformin has been a key medication for the treatment of type 2 diabetes (T2D). It is the most popular oral antihyperglycemic drug and is presently advised as first-line treatment for all newly diagnosed T2D patients (American Diabetes Association, 2014). Galegine (isoamylene guanidine), a guanidine derivative discovered in the French lilac Galega officinal is, is the original source of metformin (N, N-dimethylbiguanide), a member of the biguanide class of anti-diabetic medications (having two connected guanidine rings). Clinical research proved that topical metformin is a viable auxiliary in periodontal treatment. Apical periodontitis is retarded down in its progression by metformin's pharmacological modulation of the iNOS/NO pathway. Lipopolysaccharide (LPS)-induced iNOS expression is additionally suppressed by metformin.[8]

Midazolam

Midazolam is a benzodiazepine. Benzodiazepines belong to the group of medicines called central nervous system (CNS) depressants, which are medicines that slow down the nervous system. Induction of the sedative and anaesthetic medication midazolam (MDZ) controls inhibitory neurotransmitters in the vertebrate nervous system. In a study, by Takeo Karakida et al 2018,he demonstrated the possibility for pharmacological repositioning of MDZ for dentin regeneration. In his study he also indicated that MDZ increases the differentiation of PPU-7 cells into odontoblast and encourages the creation of hydroxyapatite that resembles dentin without utilising the database. The pharmacokinetic and pharmacological effectiveness of MDZ in animal tests needs to be clarified through more research. These findings lend credence to the dentistry field's use of MDZ to encourage dentin regeneration for endodontic procedures like pulp capping.[9]

Melatonin

The first melatonin was discovered in 1958 by Yale University School of Medicine scientists Aaron B. Lerner and his colleagues. They named the drug for its capacity to lighten the skin tone of frogs by counteracting the melanocyte-stimulating hormone's activities that cause the skin to darken. Melatonin's function in promoting sleep is perhaps its most well-

known application. The third ventricle receives melatonin from the pineal gland and releases it into circulation. Through its interactions with the suprachiasmatic nucleus of the hypothalamus and the retina, melatonin plays a role in regulating the body's sleep-wake cycles by inducing sleep and suppressing signals that promote wakefulness through its interactions with the MT1 and MT2 receptors. In dentistry, melatonin has been proven to decrease inflammation, inhibit cell growth, and control pulp cell differentiation. Melatonin boosted odontoblast activity, which caused the dental pulp to differentiate. Melatonin did not begin differentiation in undifferentiated pulp cells, but it did appear to have positive effects on periodontitis by accelerating the healing of periodontium wounds.[10, 11]

Drug Repurposing Strategy (DRS) and Management of Covid 19 - The Game Changer

Greatly enhanced older medications have historically provided some treatments for a variety of diseases. Finding repurposing drugs does not yet benefit from serendipity. Interest in drug repurposing is expanding. At present, identifying pharmacological candidates for repurposing may be done in a more logical way, especially with the use of data mining. A 2004 publication by Ashburn and Thor gave an early description of the term "drug repurposing" which seems to have marked the emergence of this relatively new idea.[12]

The COVID-19 pandemic distress on February 11th, 2020, necessitated the rapid development of viable protective methods for those who were at high risk of corona virus infection.[12] Research was conducted to facilitate the quick creation of innovative medication candidates since the discovery and development of drugs is an extended and a cumbersome procedure. The drug repurposing strategy (DRS) was used to virtually evaluate drug libraries in search of suitable drugs. This method makes use of computational methods like molecular similarity and homology modelling, to analyse the binding interaction of drug candidates with the corona virus target protein. Molecular docking studies and binding free energy calculations were also carried out to anticipate the drug-receptor interactions and binding affinities. Clinical studies were carried out in compliance with the World Health Organization's recommendations to investigate and evaluate the possible impact of already existing anti-viral medications such remdesivir, favipiravir, oseltamivir, and ritonavir on COVID-19.

In the dire circumstances, even anti-malarial medications including chloroquine phosphate and hydroxychloroquine sulphate were employed to prevent and treat COVID-19 infection. But in patients who had diseases like diabetes, hypertension, and cardiac disorders, these medications[13] could not be used effectively. Based on clinical findings, the antiviral drug favipiravir halts the replication phase of the virus life cycle, leading to a significant enhancement in the clinical treatment of covid-19. The first country to report that favipiravir has demonstrated positive clinical activity against COVID-19 was China. Its benefit to COVID-19 patients, however, was not supported by any confirmatory data.

The viral RNA-dependent RNA polymerase inhibitor, remdesivir, functions in an identical way, and it was an important drug as it played a major role during the pandemic. Consequently, remdesivir was another antiviral drug that was granted emergency approval from several regulatory bodies for COVID-19 patients. This drug is regarded as an indispensable cure for SARS-CoV-2. The drug has been demonstrated to be curative

against viruses including Ebola, Nipah, SARS-CoV-2, MERS CoV, and SARS-CoV.[14]

In Japan, the serine protease inhibitor camostatmesylate was licenced for the treatment of pancreatitis and reflux esophagitis. In human epithelial cells, research demonstrated that camostat can prevent SARS-CoV-2 entrance. However, several randomised clinical studies are presently being conducted to test the safety and effectiveness of these therapeutic compounds in COVID-19 patients.

A Janus kinase (JAK) inhibitor (JAK1/2 inhibitor), baricitinib is a small molecule that has been authorised for the treatment of rheumatoid arthritis. According to Richardson's analysis, COVID-19 treatment with baricitinib may be a good alternative.[15] It was shown that this therapeutic chemical may lower the risk of fatal admissions to critical care units. COVID-19 patients could also be treated by heparin, notably low molecular weight (LMW) heparin. In individuals with severe COVID-19, this drug may aid in halting cytokine storms. Furthermore, because of its antiviral and anti-inflammatory properties, it could contribute to reducing mortality in COVID-19 patients.[16]But further randomised clinical studies are needed to determine how well heparin works for COVID-19 patients. According to McCullough et al.'s analysis, combination/multidrug treatment is a significant priority for treating COVID-19 patients with serious illnesses.[18] Interferon’s alone or in combination with other treatments may be helpful in treating mild to moderate COVID-19 patients, according to a small number of clinical investigations.[17]

Consequently, the drug repurposing research has emerged as a time-bound and money-efficient approach for discovering novel therapeutic uses for drugs that already have FDA authorization. To combat the COVID-19 pandemic, a number of drugs that are now accessible had been repurposed for the treatment of COVID-19 patients. For the creation of COVID-19 drugs and vaccines, 4952 clinical studies had been presented at ClinicalTrials.gov until March 2021.It emerged that more than 100 nations had contributed to those clinical trials.

Conclusion

A fresh avenue for creating novel therapeutic treatments based on already-approved/existing medications is opened up by drug repurposing, which has a long history of use in fortuitous findings. As a result, the discipline of dentistry also benefits from this drug repositioning method. Dental drug repositioning can produce positive effects, but only with a thorough approach and rigorous comprehension of the details. It is important to emphasize both from a prognostic and financial standpoint how new studies in drug repurposing might overhaul the current chemotherapeutics used in dentistry.

References

1. Ashburn TT, Thor KB. Drug repositioning: Identifying and developing new uses for existing drugs. Nat Rev Drug Discov. 2004;3:673–83.
2. Liu Z, Fang H, Reagan K, Xu X, Mendrick DL, Slikker W Jr, Tong W. In silico drug repositioning: what we need to know. Drug Discov Today. 2013 Feb;18(3-4):110-5.
3. Naylor S, Schonfeld JM. Therapeutic drug repurposing, repositioning and rescue - Part I: Overview. Drug Discovery World. 2014;16:49–62.
4. Shim JS, Liu JO. Recent advances in drug repositioning for the discovery of new anticancer drugs. Int J Biol Sci. 2014 Jun 10;10(7):654-63.
5. Jin G, Wong ST. Toward better drug repositioning: prioritizing and integrating existing methods into efficient pipelines. Drug Discov Today. 2014 May;19(5):637-44.

6. Abd Rahman F, Mohd Ali J, Abdullah M, Abu Kasim NH, Musa S. Aspirin Enhances Osteogenic Potential of Periodontal Ligament Stem Cells (PDLSCs) and Modulates the Expression Profile of Growth Factor-Associated Genes in PDLSCs. J Periodontol. 2016 Jul;87(7):837-47.
7. Yuan M, Zhan Y, Hu W, Li Y, Xie X, Miao N, Jin H, Zhang B. Aspirin promotes osteogenic differentiation of human dental pulp stem cells. Int J Mol Med. 2018 Oct;42(4):1967-1976.
8. Divya TC, Muddappa SC, Singh P, Rajan RR, Remya M, Sreehari D. Drug Repurposing for Tooth Regeneration: The Promising Premises. J Pharm Bioallied Sci. 2021 Nov;13
9. Karakida T, Onuma K, Saito MM, Yamamoto R, Chiba T, Chiba R, Hidaka Y, Fujii-Abe K, Kawahara H, Yamakoshi Y. Potential for Drug Repositioning of Midazolam for Dentin Regeneration. Int J Mol Sci. 2019 Feb 4;20(3):670.
10. Zhao D, Yu Y, Shen Y, Liu Q, Zhao Z, Sharma R, Reiter RJ. Melatonin Synthesis and Function: Evolutionary History in Animals and Plants. Front Endocrinol (Lausanne). 2019 Apr 17;10:249.
11. Pandi-Perumal SR, Trakht I, Srinivasan V, Spence DW, Maestroni GJ, Zisapel N, Cardinali DP. Physiological effects of melatonin: role of melatonin receptors and signal transduction pathways. Prog Neurobiol. 2008 Jul;85(3):335-53.
12. Sahoo BM, Ravi Kumar BVV, Sruti J, Mahapatra MK, Banik BK, Borah P. Drug repurposing strategy (DRS): Emerging approach to identify potential therapeutics for treatment of novel coronavirus Infection. Front Mol Biosci. 2021;Feb;8:628144.
13. Vincent MJ, Bergeron E, Benjannet S, Erickson BR, Rollin PE, Ksiazek TG, Seidah NG, Nichol ST. Chloroquine is a potent inhibitor of SARS coronavirus infection and spread. Virol J. 2005 Aug 22;2:69.
14. Malin JJ, Suárez I, Priesner V, Fätkenheuer G, Rybniker J. Remdesivir against COVID-19 and Other Viral Diseases. Clin Microbiol Rev. 2020 Oct 14;34(1):e00162-20.
15. Richardson P, Griffin I, Tucker C, Smith D, Oechsle O, Phelan A, Rawling M, Savory E, Stebbing J. Baricitinib as potential treatment for 2019-nCoV acute respiratory disease. Lancet. 2020 Feb 15;395(10223):e30-e31.
16. McCullough PA, Alexander PE, Armstrong R, Arvinte C, Bain AF, Bartlett RP, Berkowitz Multifaceted highly targeted sequential multidrug treatment of early ambulatory high-risk SARS-CoV-2 infection (COVID-19).Rev Cardiovasc Med. 2020 Dec 30;21(4):517-530.
17. Fu W, Liu Y, Xia L, Li M, Song Z, Hu H, Yang Z, Wang L, Cheng X. A clinical pilot study on the safety and efficacy of aerosol inhalation treatment of IFN-κ plus TFF2 in patients with moderate COVID-19. EClinicalMedicine. 2020 Aug;25:100478.