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Artificial Intelligence approach to verify irrationality of FDCs listed by CDSCO

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ABSTRACT

Various Artificial Intelligence (AI) tools were utilized to verify the irrationality of Fixed-Dose-Combinations (FDCs) which were already proven irrational by CDSCO. SwissADME, one of the AI tools was able to generate properties of FDCs by using two-dimensional structures downloaded from Pubchem (a free data source). Another interesting finding was obtained by using two different AI tools ChatGPT and BARD. These AI tools identified uncommon comparative properties and predicted most of the FDCs are irrational. This suggests that these AI tools can play a crucial role in identifying irrationality in drugs. Additionally, the study looked into drug-drug interactions, and it was found that most of the FDCs are exhibited such interactions. AI tools were capable of analysing the irrationality of a significant number of drugs. However, SwissADME, one of the AI tools has limited capability in processing large structures. This proves the further need for improvements in AI technology to produce more accurate and comprehensive analyses.

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INTRODUCTION

Artificial Intelligence

Artificial intelligence (AI) is a field of study and engineering that involves the creation of intelligent machines, particularly advanced computer programs. While it shares similarities with the aim of comprehending human intelligence using computers, AI is not limited to biologically observable methods (Sharma & Bharatam, 2022). However, historically, AI has been primarily applied in specific and specialized domains (Sellwood *et al.*, 2018). Artificial intelligence (AI) encompasses various methodological domains, including reasoning, knowledge representation, solution search, and, notably, machine learning (ML) as a fundamental paradigm. AI employs systems and software that can analyse and learn from input data to autonomously make decisions and achieve specific objectives (Paul *et al.*, 2020). The primary goal of AI is to identify information processing challenges and provide abstract strategies to solve them (Krishnaveni *et al.*, 2019). AI and deep learning have proven valuable in addressing critical problems that are time-consuming for humans (Chaudhari & Patel, 2020). The increasing use of AI is poised to bring about changes in clinical examination and training methodologies (Patel & Shah, 2022). In the realm of clinical development, AI tools like natural language processing (NLP) and computer vision can integrate

omics data, electronic health records (EHR), and biomarkers to identify and characterize appropriate subpopulations for trials (Jang, 2019). Pharmaceutical companies such as Bayer, Roche, and Pfizer are collaborating with information technology (IT) companies to develop AI-based methods for drug design. Notably, In-silico Medicine, aided by AI, discovered a drug for idiopathic pulmonary fibrosis, which showed promising results in Phase I trials (source: <https://clinicaltrials.gov/ct2/show/NCT05154240>) (Chen *et al.*, 2023). Consequently, AI is revolutionizing the healthcare sector, but its true impact is yet to be fully realized (Agrawal, 2018).

SwissADME

SwissADME is an accessible web tool that provides users with a range of fast and reliable predictive models for physicochemical properties, pharmacokinetics, drug-likeness, and medicinal chemistry suitability. These models include in-house methods such as BOILED EGG, iLOGP, and bioavailability radar (Diana *et al.*, 2017). The tool requires input molecules to be listed with one molecule per line, using the simplified molecular input line entry system (SMILES) (Mahanthesh *et al.*, 2020). The SwissADME online tool offers a reliable option for designing drugs by utilizing either natural products or synthetic compounds. This tool aids in identifying a specific set of compounds suitable for future experimental studies on

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aspects such as pharmacokinetics, bioavailability, and other factors crucial for the development of novel drugs.

ChatGPT

ChatGPT is an AI chatbot tool that utilizes a large language model trained on vast amounts of internet data (Lubowitz, 2023). As a generative language model, ChatGPT has numerous potential applications in education, including generating realistic patient case scenarios, personalizing learning experiences, and enhancing medical textbooks (Eysenbach, 2023). It is widely used for determining the drug-likeness profile of compounds by incorporating Lipinski's rule, which assesses the likelihood of orally active substances becoming effective oral drugs based on physicochemical parameters (Al Azzam, 2022). The GPT architecture employs a neural network to process natural language and generate responses that are contextually relevant to the input text (Sallam, 2023).

Bard

On February 7, 2023, Google officially debuted BARD, its AI technology, with the goal of competing with Open AI's well-known ChatGPT – 3 language model (Ram, 2023). The scientific possibilities of Bard are extensive. Bard offers the potential for automating numerous scientific endeavours, such as analysing data, designing experiments, reviewing the literature, and writing scientific papers (Siad, 2023).

MATERIALS AND METHODS

Inclusion Criteria

16 FDCs in 294 FDCs enlisted in the CDSCO list were recommended as irrational by Prof. Kokate Committee (Table 1). By using AI tools here, we are analysing 11 of 16 FDCs recommended as irrational by CDSCO (CDSCO, 2023).

Prediction Analysis

Two dimensional structures of FDCs were downloaded from Pubchem, a free data resource. In silico screening of FDCs was conducted using the free web tool SwissADME (<http://www.swissadme.ch/index.php#>), which uses the ADME properties of compound as estimates and indicators of pharmacokinetics and drug-likeness of a compound (Rana & Prakash, 2021). In addition, another free AI tool ChatGPT and BARD was used to analyse the properties of the 11 FDCs that are recommended as irrational by CDSCO.

RESULT AND DISCUSSION

1. Acetyl salicylic acid + Ethoheptazine

SwissADME analysis

It was observed that both acetylsalicylic acid (ASA) and ethoheptazine show variance in the inhibition of the CYP2D6. CYP2D6 was inhibited by Ethoheptazine whereas ASA was

unable to inhibit it. Moreover, there was a slight variance in the skin permeation of both drugs.

ChatGPT analysis

It was observed that both drugs are rapidly absorbed in the GI tract with peak plasma concentration achieved within 1-2 hrs after oral administration. But ASA has a relatively large volume of distribution as compared to Ethoheptazine. Moreover, ASA is primarily eliminated by hepatic metabolism and the other is eliminated through renal excretion of metabolites. The elimination half-life of the ASA is relatively short, approximately 15-20 minutes. However, the elimination half-life of its active metabolite is much longer ranging from 2-3 hrs to 15-30 hrs whereas the elimination half-life of ethoheptazine is 10-20 hrs and its metabolite is approximately 30-40 hrs depending upon the dose.

Bard analysis

Bard predicted that when these two drugs are combined, they do not provide any additional benefit over aspirin alone. In fact, the combination may actually increase the risk of side effects, such as stomach bleeding, liver damage, and kidney damage. Moreover, The American Medical Association (AMA) has classified the combination of aspirin and ethoheptazine as an "irrational mixture." This means that the combination is not supported by scientific evidence and should not be used.

Drug – Drug interaction

The major interactions shown by ChatGPT are increased risk of bleeding, central nervous system depression and gastrointestinal side effects such as stomach irritation, ulceration and bleeding. On the other hand, Bard analysed that the combination of this mixture may cause stomach bleeding, liver damage, kidney damage, allergic reactions, dizziness, seizures, coma, hypertension, blurred vision, etc.

2. Dicyclomine + Paracetamol + Clidinium Bromide

SwissADME analysis

It was observed that there was a variance in the BBB permeation of paracetamol and clidinium bromide. Moreover, paracetamol is not a p – gp substrate while the clidinium bromide is a substrate of p – gp. On the other hand, SwissADME was unable to analyse the pharmacokinetic properties of dicyclomine. In addition, SwissADME was unable to generate the response for dicyclomine.

ChatGPT analysis

It was observed that there was a variance in the pharmacokinetic properties such as metabolic pathway and elimination half-life of this FDC. Paracetamol is metabolized in the liver by two pathways (glucuronidation and sulfation), clidinium bromide is metabolized by various pathways, including hydrolysis, N- dealkylation and oxidation in the liver whereas dicyclomine

was metabolized in the liver primarily through cytochrome P450 enzymes and the elimination half-life of paracetamol, clidinium bromide and dicyclomine is 2-3 hrs in adults, 2-4 hrs and 1-1.5 hrs respectively. Some of the other considerations are overlapping effects, increased anticholinergic effects, limited efficacy, and individual treatment for patients.

Bard analysis

It was observed that when dicyclomine, paracetamol, and clidinium bromide are combined together, they can cause a number of side effects, including dry mouth, blurred vision, constipation, and drowsiness. In some cases, the combination can also cause more serious side effects, such as heart problems and seizures. The risks of the combination outweigh the benefits because the combination does not provide any additional relief that cannot be achieved with the individual medications. In fact, the combination may actually make the side effects worse.

Drug – Drug interaction

Drugs.com predicted moderate drug-drug interaction between dicyclomine and clidinium bromide showing excessive parasympatholytic effects (paralytic ileus, hyperthermia, heat stroke, etc.), peripheral symptoms of intoxication (mydriasis, blurred vision, dry skin, tachycardia etc.), tardive dyskinesia, hallucinations, hyperactivity, etc., and both clidinium bromide and dicyclomine may also cause decreased gastrointestinal absorption of acetaminophen.

3. Gliclazide + Chromium picolinate

SwissADME analysis

It was observed that both Gliclazide and Chromium Picolinate have variances in GI absorption. It was shown that Gliclazide has higher absorption as compared to chromium picolinate. Moreover, gliclazide is a substrate of p-gp while the latter is not.

ChatGPT analysis

There was a huge variance observed in the pharmacokinetic properties of gliclazide and chromium picolinate. Gliclazide has a moderate volume of distribution and is primarily bound to albumin and the bound fraction is around 90% whereas chromium has low tissue binding and is mainly bound to transferrin and has been detected in various tissues, including the liver, kidney, muscle and bone. Gliclazide is extensively metabolized in the liver. The primary metabolic pathway is through oxidation, primarily mediated by the cytochrome P450 enzyme CYP2C9. The main metabolites formed are inactive and do not contribute significantly to the pharmacological activity of gliclazide. Chromium picolinate undergoes minimal metabolism in the body. It is primarily excreted unchanged or as a metabolite in the urine. Gliclazide and its metabolites are primarily eliminated via the kidneys. The elimination half-life of gliclazide is relatively short, ranging from 10 to 20 hours. Less than 1% of the administered dose is excreted unchanged in the urine, indicating extensive metabolism. The elimination

half-life of chromium is relatively short, ranging from several hours to a few days. Chromium is primarily excreted via the kidneys, both in its original form and as metabolites. The extent of urinary excretion varies depending on the dose and duration of supplementation.

Bard analysis

Bard predicted that gliclazide is a type of medication called sulfonylurea, which works by stimulating the pancreas to produce more insulin. Chromium picolinate is a mineral that is sometimes marketed as a dietary supplement for improving blood sugar control. However, there is no scientific evidence to support this claim. In fact, some studies have shown that chromium picolinate may actually have negative effects on blood sugar control. The combination of these two drugs does not provide any additional benefit over using gliclazide alone, and may actually be harmful. The combination of these drugs may cause a negative effect on blood sugar control such as hypoglycemia.

Drug - Drug interaction

When the drug interaction was checked in ChatGPT it was observed that chromium picolinate enhances insulin sensitivity and affects glucose metabolism, which may potentially impact the efficacy and safety of antidiabetic medications such as gliclazide. Therefore, it is advisable to exercise caution and consider potential interactions between these two substances.

4. Paracetamol + Lignocaine

SwissADME analysis

It was observed that both the drugs have high GI absorption and both drugs can show BBB permeation. However, paracetamol does not show inhibition of CYP2D6 and Lignocaine inhibits this cytochrome.

ChatGPT analysis

It was observed that paracetamol is rapidly or completely absorbed through the GI tract with a peak plasma concentration of 30 to 60 min whereas lidocaine can be administered through various routes, including topically (poorly absorbed), intravenous and subcutaneous (rapidly absorbed into systemic circulation). Moreover, 10% to 25% of paracetamol is bound to plasma proteins and approximately 60% to 80% of lidocaine in the bloodstream is bound to plasma proteins. The elimination half-life of paracetamol and lignocaine is about 2-3 hrs and 1.5-2 hrs respectively.

Bard analysis

The combination of paracetamol and lignocaine is considered an irrational drug combination. When used together, they do not provide any additional benefit but in fact, may actually increase the risk of serious side effects. Moreover, it was observed that these drugs do not have any synergistic effects and lignocaine can increase the risk of liver damage when used with paracetamol.

Drug – Drug interaction

On checking the interaction between these drugs on AI drug interaction checker tools such as drugs.com, Medscape and WebMD, it was observed that there were no possible interactions found between these drugs.

5. Cefadroxil and probenecid

SwissADME analysis

It was observed that cefadroxil has low GI absorption as compared to probenecid. Both the drugs do not show BBB permeation and there was slight variation in the skin permeation of the drugs.

ChatGPT analysis

It was observed that cefadroxil reaches its peak plasma concentration within 1-2hrs and Food does not significantly affect its absorption whereas probenecid peak plasma concentrations within 2-4 hours. It is recommended to take probenecid with food to reduce gastrointestinal side effects. Moreover, Cefadroxil has a moderate volume of distribution and penetrates well into body tissues and fluids, including the respiratory tract, skin, and urine whereas probenecid has a relatively small volume of distribution, and it does not penetrate well into certain tissues, such as the central nervous system.

Bard analysis

Bard predicted that when cefadroxil and probenecid are taken together, the probenecid can increase the amount of cefadroxil that is absorbed into the bloodstream. This can lead to higher-than-normal levels of cefadroxil in the blood, which can increase the risk of side effects such as gastrointestinal upset, rash, dizziness, fatigue, and allergic reactions.

Drug - Drug interaction

On checking the drug interaction on Medscape, it was observed that cefadroxil will increase the level or effect of probenecid by acidic (anionic) drug competition for renal tubular clearance while on checking the interaction on drugs.com, it was observed that coadministration with probenecid may increase and prolong the serum concentrations of some cephalosporins.

6. Cefuroxime and Serratiopeptidase

ChatGPT analysis

Cefuroxime and serratiopeptidase are not typically prescribed together because they have different mechanisms of action and are used to treat different conditions. Cefuroxime is an antibiotic that belongs to the class of drugs known as cephalosporins. It is commonly used to treat bacterial infections such as respiratory tract infections, urinary tract infections, and skin and soft tissue infections. Cefuroxime works by inhibiting the growth and multiplication of bacteria. Serratiopeptidase, on the other hand,

is an enzyme derived from the bacteria *Serratia marcescens*. It has anti-inflammatory and fibrinolytic properties, meaning it helps reduce inflammation and dissolve fibrin, a protein involved in blood clotting. Serratiopeptidase is sometimes used as a supplement for its potential benefits in reducing swelling and improving tissue healing. Since cefuroxime is an antibiotic used to treat bacterial infections, and serratiopeptidase is an enzyme with anti-inflammatory properties, they target different aspects of health conditions. There is generally no specific therapeutic benefit of combining these two drugs, as they do not have a synergistic effect or interact in a way that enhances their effectiveness. Furthermore, combining drugs unnecessarily may increase the risk of side effects and drug interactions.

Bard analysis

Bard predicted that the combination of cefuroxime and serratiopeptidase is considered to be an irrational drug combination. There is no evidence that serratiopeptidase is effective in treating bacterial infections, and it may actually interfere with the effectiveness of antibiotics. Additionally, serratiopeptidase can cause side effects, such as bleeding, bruising, and allergic reactions.

7. Amoxicillin + Serratiopeptidase

ChatGPT analysis

It was observed that both drugs are shown as irrational drug combinations by ChatGPT (Figure 1). Amoxicillin is an antibiotic that is commonly prescribed to treat bacterial infections. It works by inhibiting the growth of bacteria and interfering with their cell wall synthesis whereas serratiopeptidase, on the other hand, is an enzyme with anti-inflammatory properties. It is used to reduce inflammation and swelling, often in conditions unrelated to bacterial infections.

Bard analysis

When these drugs are together, it was observed that patients who were given amoxicillin and serratiopeptidase were more likely to experience side effects such as diarrhoea, nausea, and vomiting than patients who were given amoxicillin alone. The study also found that the combination of amoxicillin and serratiopeptidase was no more effective at clearing up infections than amoxicillin alone. Another study found that patients who were given amoxicillin and serratiopeptidase were more likely to develop antibiotic resistance than patients who were given amoxicillin alone.

8. Dicyclomine + Paracetamol + Clidinium bromide + Chlordiazepoxide

ChatGPT analysis

ChatGPT predicted this combination as an irrational drug combination. This prediction was made on the basis of the different pharmacological actions and mechanisms of action. Moreover, it was observed that the inclusion of multiple

medications from different drug classes, such as anticholinergics (dicyclomine, clidinium bromide), analgesics (paracetamol), and benzodiazepines (chlordiazepoxide), without a clear medical indication or proper supervision can increase the risk of adverse effects, drug interactions, and potential misuse. Additionally, the combination of chlordiazepoxide (a benzodiazepine) with other central nervous system depressants like anticholinergics (dicyclomine, clidinium bromide) can have additive sedative effects, leading to increased drowsiness and impaired cognitive function.

Bard analysis

It was shown that the combination of dicyclomine, paracetamol, clidinium bromide, and chlordiazepoxide is considered an irrational drug combination. There is no evidence that combining these four medications provides any additional benefit over taking any one of them alone. Some studies have shown that combining these medications can increase the risk of side effects.

9. Amoxicillin + Serratiopeptidase + Lactobacillus Sporogens

ChatGPT analysis

ChatGPT was unable to accurately predict the rationality or irrationality of this drug combination. The response generated was shown in Figure 2.

Bard analysis

Bard predicted this drug combination as an irrational drug combination. It was observed that serratiopeptidase and

Yes, the combination of amoxicillin and serratiopeptidase is generally considered an irrational drug combination. These two medications have different mechanisms of action and are typically used for different purposes.

Figure 1: ChatGPT prediction on FDC of amoxicillin and serratiopeptidase

A is amoxicillin and serratiopeptidase and lactobacillus sporogens an irrational drug combination?

The combination of amoxicillin, serratiopeptidase, and Lactobacillus sporogens does not have an established consensus on its rationality or irrationality as a drug combination. It's important to note that the rationality of a drug combination depends on several factors, including the specific medical condition being treated, the patient's medical history, and the rationale provided by the prescribing healthcare professional.

Amoxicillin is an antibiotic used to treat bacterial infections, serratiopeptidase is an enzyme with potential anti-inflammatory properties, and Lactobacillus sporogens is a probiotic strain that helps maintain a healthy balance of gut bacteria. Each component of this combination serves a different purpose and may have individual benefits.

It is possible that this combination is being prescribed for a particular reason based on the patient's specific condition, symptoms, or medical history. It is crucial to consult with a healthcare professional or pharmacist who can evaluate your specific circumstances and provide guidance on the rationality and safety of this particular drug combination for you. They have access to your medical records and can offer personalized advice based on your individual needs.

Regenerate response

Figure 2: Chatgpt prediction on FDC of amoxicillin, serratiopeptidase and lactobacillus sporogens

lactobacillus sporogenes may actually interfere with the effectiveness of amoxicillin and also there is no evidence that serratiopeptidase or lactobacillus sporogenes provide any additional benefit over taking amoxicillin alone.

Drug – Drug interaction

On checking the drug interaction on drugs.com it was observed that coadministration of oral probiotic preparations with oral antibiotics may reduce the efficacy of the probiotic. It has been theorized that concomitant antibiotics may kill the live organisms found in lactobacillus, bacillus coagulans, and bifidobacteria containing oral probiotic preparations.

10. Amoxicillin + cloxacillin + lactic acid bacillus + Serrapeptase

ChatGPT Analysis

ChatGPT predicted this drug combination as an unusual drug combination and potentially uncommon. Additionally, the rationality of combining these medications depends on various factors, including the specific condition being treated, the patient's medical history, and the rationale provided by the prescribing healthcare professional. There may be specific circumstances or indications where this combination is considered appropriate.

Bard analysis

Bard predicted that the combination of amoxicillin and cloxacillin is unnecessary, as they are both penicillin antibiotics that work in the same way. The addition of lactic acid bacillus and serrapeptase is also unnecessary, as there is no evidence that these supplements offer any benefit in the treatment of bacterial infections. In fact, there is some concern that serrapeptase may actually increase the risk of bleeding. Moreover, it was observed that The World Health Organization (WHO) has developed a list of irrational drug combinations that should be avoided.

Table 1: List of 16 FDCs in 294 FDCs recommended as irrational by Prof. Kokate Committee

S. No.	NAME of FDCs
1	Acetyl Salicylic Acid+ Ethoheptazine
2	Aloe extract+Allantoin+ alpha tocopherol acetate+ D- Panthenol+ Vitamin A
3	Aloe Extract+ Vitamin E +Dimethicone+ Glycerine
4	Aloe vera+Jojoba Oil+ Vitamin E
5	Aloe Vera+Orange Oil
6	Aloe Vera+Jojoba Oil+Wheat Germ Oil+Tea Tree Oil
7	Aloe Vera+ Vitamin E +Herbal
8	Dicyclomine+ Paracetamol+ Clidinium Bromide
9	Dicyclomine+ Paracetamol+ Clidinium Bromide+ Chlordiazepoxide
10	Gliclazide+ Chromium Picolinate
11	Paracetamol+ Lignocaine
12	Amoxicillin+ Serratiopeptidase+ Lactobacillus Sporogens
13	Amoxicillin+ Cloxacillin+ Lactic Acid Bacillus+ Serrapeptase
14	Amoxicillin+ Serratiopeptidase
15	Cefadroxil+ Probenecid
16	Cefuroxime+ Serratiopeptidase

Table 2: Prediction result of the FDCs that are considered irrational by CDSCO

S. No.	Name of FDC	SwissADME	ChatGPT	Bard	Drug interaction
1	Acetyl Salicylic acid+Ethoheptazine	Yes	Yes	Yes	Yes
2	Dicyclomine+paracetamol+clidinium bromide	Yes	Yes	Yes	Yes
3	Gliclazide+chromium picolinate	Yes	Yes	Yes	Yes
4	Paracetamol+lignocaine	Yes	Yes	Yes	No
5	Cefadroxil+probenecid	Yes	Yes	Yes	Yes
6	Cefuroxime+serratiopeptidase	NA	Yes	Yes	NA
7	Amoxicillin+serratiopeptidase	NA	Yes	Yes	NA
8	Dicyclomine+paracetamol+clidinium bromide+chlordiazepoxide	NA	Yes	Yes	NA
9	Amoxicillin+serratiopeptidase+lactobacillus sporogens	NA	NA	Yes	Yes
10	Amoxicillin+cloxacillin+lactic acid bacillus+Serrapeptase	NA	Yes	Yes	Yes
11	Aloe vera+orange oil	NA	Yes	Yes	Yes

This list includes amoxicillin + cloxacillin + lactic acid bacillus + Serrapeptase.

Drug - Drug interaction

On checking the drug interaction on drugs.com, it was observed that the coadministration of oral probiotic preparations with oral antibiotics may reduce the efficacy of the probiotic. It has been theorized that concomitant antibiotics may kill the live organisms found in lactobacillus, bacillus coagulans, and bifidobacteria containing oral probiotic preparations.

11. Aloe vera + orange oil

ChatGPT analysis

It was observed that aloe vera and orange oil are two different substances used for different purposes. While they can both have potential benefits, there may not be a strong rationale for combining them directly. Aloe vera is commonly used for its moisturising and soothing properties, often applied topically to the skin whereas orange oil is an essential oil extracted from the peels of oranges. It is often used for its pleasant scent and can be used in aromatherapy or as a flavouring agent. It is not typically used topically for skincare purposes or ingested orally. In addition, orange oil can also cause skin irritation and allergic reactions when applied topically.

Bard analysis

It was observed that this combination could actually be harmful. Aloe vera can increase the absorption of orange oil into the skin, which could lead to skin irritation or allergic reaction.

Drug – Drug interaction

When checked on Bard, it was observed, drug interaction can cause an increased risk of bleeding, sun sensitivity and liver damage.

AI Tools Prediction Result of FDC

When the FDCs were analysed by using various AI tools, it was observed that most FDCs share dissimilar properties and have drug–drug interaction between them (Table 2). AI tools also

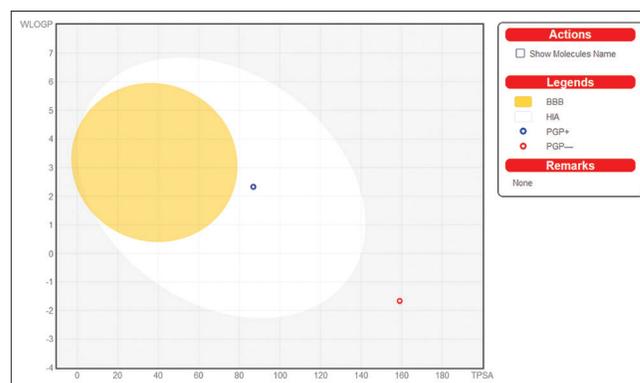


Figure 3: Incompatible FDC shown by SwissADME

predicted that there is no significant relevance in taking these combinations together.

In Figure 3, the blue dot represents Molecule 1 and the red dot represents Molecule 2. It is clearly shown that both drugs have different pharmacokinetic properties. Molecule 1 is a substrate of p-gp and has better gastrointestinal absorption as compared to Molecule 2. However, both drugs are BBB impermeant.

CONCLUSION

In this study, various AI tools were utilized to analyse the irrationality of the FDC. SwissADME was able to generate the properties of 5 FDCs out of 11 and the variance was found in most of the drugs. However, the inability to process drugs carrying large structures proves the limited capability of these AI tools. Moreover, it was observed that both ChatGPT and BARD have shown surprising results. They predicted most of these drugs as irrational and shared uncommon properties. Another aspect of this study includes drug–drug interaction and it was found in most of FDC. AI tools were significantly able to analyse irrationality in most of the FDCs, however, there is still a gap for improvement exists. After filling that gap, more accurate and impactful results could be generated.

REFERENCES

Agrawal, P. (2018). Artificial Intelligence in Drug Discovery and Development. *Journal of Pharmacovigilance*, 6(2), 1-2. <https://doi.org/>

- org/10.4172/2329-6887.1000e173
- Al Azzam, K. M. (2022). SwissADME and pkCSM Webservers Predictors: an integrated Online Platform for Accurate and Comprehensive Predictions for In Silico ADME/T Properties of Artemisinin and its Derivatives. *Complex Use Mineral Resources*, 325(2), 14-21. <https://doi.org/10.31643/2023/6445.13>
- CDSCO. (2023). Central Drugs Standard Control Organization. Retrieved from: https://cdsco.gov.in/openncms/openncms/system/modules/CDSCO.WEB/elements/download_file_division.jsp?num_id=MTAwMDY=
- Chaudhari, M. K., & Patel, V. P. (2020). A REVIEW ARTICLE ON ARTIFICIAL INTELLIGENCE; Change in Modern Techniques of pharmaceutical Formulation and Development. *Journal of Emerging Technologies and Innovative Research*, 7(9), 1466-1473.
- Chen, W., Liu, X., Zhang, S., & Chen, S. (2023). Artificial Intelligence for drug discovery: Resources, methods, and applications. *Molecular Therapy: Nucleic Acids*, 31, 691-702. <https://doi.org/10.1016/j.omtn.2023.02.019>
- Diana, A., Michielin, O., & Zoete, V. (2017). SwissADME: a free web tool to evaluate pharmacokinetics, drug-likeness and medicinal chemistry friendliness of small molecules. *Scientific Reports*, 7, 42717. <https://doi.org/10.1038/srep42717>
- Eysenbach, G. (2023). The Role of ChatGPT, Generative Language Models, and Artificial Intelligence in Medical Education: A Conversation with ChatGPT and a call for Papers. *Journal of Medical Internet Research Medical Education*. <https://doi.org/10.2196/46885>
- Jang, I.-J. (2019). Artificial intelligence in drug development: clinical pharmacologist perspective. *Translation and Clinical Pharmacology*, 27(3), 87-88. <https://doi.org/10.12793/tcp.2019.27.3.87>
- Krishnaveni, C., Arvapalli, S., Sharma, J. V. C., & Divya, K. (2019). Artificial Intelligence in Pharma Industry - A Review. *International Journal of Innovative Pharmaceutical Sciences and Research*, 7(10), 37-50.
- Lubowitz, J. H. (2023). ChatGPT, An Artificial intelligence Chatbot, Is Impacting Medical Literature. *Arthroscopy: The Journal of Arthroscopic and Related Surgery*, 39(5), 1121-1122. <https://doi.org/10.1016/j.arthro.2023.01.015>
- Mahantesh, M. T., Ranjith, D., Yaligar, R., Jyothi, R., Narappa, G., & Ravi, M. V. (2020). Swiss ADME prediction of phytochemicals present in *Butea monosperma* (Lam.) Taub. *Journal of Pharmacognosy and Phytochemistry*, 9(3), 1799-1809.
- Patel, V., & Shah, M., (2022). Artificial intelligence and machine learning in drug discovery and development. *Intelligent Medicine*, 2(3), 134-140. <https://doi.org/10.1016/j.imed.2021.10.001>
- Paul, D., Sanap, G., Shenoy, S., Kalyane, D., Kalia, K., & Tekade, R. K. (2020). Artificial Intelligence in drug discovery and development. *Drug Discovery Today*, 26(1), 80-93. <https://doi.org/10.1016/j.drudis.2020.10.010>
- Ram, B., & Verma, P. (2023). Artificial Intelligence AI-based Chatbot study of Chatbot, Google AI Bard and Baidu Ai. *World Journal of Advanced Engineering Technology and Sciences*, 8(1), 258-261. <https://doi.org/10.30574/wjaets.2023.8.1.0045>
- Rana, S., & Prakash, P. (2021). In Silico pharmacokinetic Prediction for New Fixed Dose Combinations - A Lesson to Learn. *Inventi Rapid: Pharmacokinetics & Pharmacodynamics*, 2021(2), 1-8.
- Sallam, M. (2023). ChatGPT Utility in Healthcare Education, Research, and Practice: Systematic Review on the Promising Perspectives and Valid Concerns. *Healthcare*, 11(6), 887. <https://doi.org/10.3390/healthcare11060887>
- Sellwood, M. A., Ahmed, M., Segler, M. H. S., & Brown, N. (2018) Artificial Intelligence in drug discovery. *Future Medicinal Chemistry*, 10(17), 2025-2028. <https://doi.org/10.4155/fmc-2018-0212>
- Sharma, V. K., & Bharatam, P. V. (2022). Artificial Intelligence in Drug Discovery (AIDD). *Current Research & Information on Pharmaceutical Sciences*, 16(1), 3-7.
- Siad, S. M. (2023). The Promise and Perils of Google's Bard for Scientific Research. *Humanities commons*. <https://doi.org/10.17613/yb4n-mc79>