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Research Article
An *in silico* Modeling for the Prediction of Propranolol-Omniscan Interaction

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Abstract

Background and Objective: Propranolol is an agent which blocks β-adrenergic stimuli via the inhibition of β-adrenergic receptors in the myocardial, bronchial and smooth muscle regions. When using it with other agents such as Omniscan, various contradictions can occur as a risk to Propranolol pharmacokinetics and metabolism. This study was conducted to predict the effects of co-administration of both agents, Propranolol and Omniscan, respectively. **Materials and Methods:** ChemDIS-Mixture (v.5.0) was used for the prediction and identification of various effects caused by the co-administration of both agents. The confidence score was adjusted to medium (0.4), while the level of significance was set at 0.05, using Benjamini-Hochberg multiple test correction. **Results:** The findings of the predictive analysis revealed that the co-administration of Propranolol and Omniscan produced several effects in the human body, including the involvement of various proteins, molecular pathways and diseases. 04 new signalling pathways, 08 GO terms, 17 DO terms as well as 21 DOLite terms. **Conclusion:** The use of Propranolol should be considered before the administration of Omniscan in patients scheduled for MRI examinations to avoid unprecedented effects in the body as well as serious complications in diseased patients caused due to Drug-Drug Interactions (DDIs).

Key words: Magnetic resonance imaging, omniscan, propranolol, drug-drug interaction, toxic effects, chemdis-mixture

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Data Availability: All relevant data are within the paper and its supporting information files.

INTRODUCTION

Conventional pharmacology relies on its focus on the effects of various drugs and their relative proportion to their concentrations as well as the interactions of drugs with their receptors. Normally, receptor sites are those which are usually not easy to access, due to which drug concentrations present in body fluids are employed for the correlation with the drug effect and subsequent modelling. Drug plasma concentrations are generally quantified and are used as an alternative to drug concentrations as the former is attributable for maintaining the balance of drug concentration in other parts of the human body. The pharmacokinetics of drugs involve the measurement of drugs and their concentration in body fluids, which is then ultimately used in the making of mathematical models, deducing interactions of the drugs with various receptors and their sites as well as the interactions of the drug with the body. Complications, side effects or secondary interactions may arise if two or more drugs interact with each other, affecting the pharmacokinetic behaviour of one drug or both. These interactions, known as drug-drug interactions (DDIs), can also be the outcome of the antagonism caused by one drug when taken with another drug and vice versa[1].

Propranolol is a β-adrenergic antagonist which has been used in the treatment of various medical conditions such as heart failure, tachycardia, cardiovascular disease, atrial fibrillation as well as coronary artery disease. Moreover, they have also been prescribed to be used against hypertension along with the aforementioned heart conditions and complications[2]. Its widespread uses also range to treat non0cardiovascular conditions, such as Restless Leg Syndrome (RLS), neurological tremors as well as anxiety as tachycardia is often considered to be a sub-set symptom of anxiety and other mental disorders[3]. The activation of β-1 receptors leads to the increment in cyclic AMP (cAMP), which increases calcium present at an intracellular level, in turn increasing the contraction of muscle fibres. Blockage of β-adrenergic receptors ultimately results in the reduction in the heart workload and oxygen demand[4]. As is the case with most drugs, β-blockers are broken down primarily in the liver, after which less than half of the administered drug tends to reach systemic circulation[5]. Propranolol is actively metabolized by 4-hydroxypropranolol, formed fromCYP2D6 enzyme[6]. This metabolism occurs in the liver and the drug has a reported half-life of approximately 3-6 hrs[7].

Propranolol is absorbed and present in the plasma after 30 min of oral administration, whereas peak concentrations appear after 60-90 min. Moreover, Propranolol hydrochloride is another form of Propranolol that is absorbed approximately 6 hrs after the administration of the drug. Propranolol is then distributed throughout the body, into various body parts such as lungs, kidneys, heart as well as liver. It is also capable of crossing the blood-brain barrier as well as the placenta and breast milk, meaning that after administration in pregnant women the drug can cross over to the fetus as well as through mother's milk to the newborn child. The distributive amount and value of Propranolol at a given rate is subject to vary in proportion to the amount of drug present in its unbound form in the patient's blood. Most of the Propranolol tends to bind with proteins found in the plasma over a wider range of blood concentrations. Hence, the drug can be metabolized in the human body in both its bound and unbound forms, where the increased binding of the plasma and protein with the drug, in turn, leads to the increase in its metabolism, thereby reducing its distributive volume and giving it a much shorter half-life[8].

Omniscan (DrugBank Acc. No: DB00225), the commercial name for the contrast agent known as Gadodiamide, is a gadolinium-based contrast agent which aids in the visualization of vascularity in contrast-based imaging examinations, such as magnetic resonance imaging (MRI). It has been reported that the co-administration of Omniscan in patients taking Propranolol reduces the excretory rate of the latter, resulting in an elevated serum level in the body[8].

This study was conducted to predict the effects of the co-administration of Propranolol with Omniscan, a gadolinium-based Magnetic Resonance Imaging (MRI) contrast agent as well as the biological pathways, diseases and related genes that were affected by the interaction of both drugs. The analysis was performed using ChemDIS-Mixture, which is an online tool that sequesters data from extensively curated online databases of diseases, pathways, proteins and helps to decipher the possible interactions between two drugs.

MATERIALS AND METHODS

Study area: This study was carried out from August, 2020 to April, 2021 in the Laboratory of Molecular Simulations, Department of Medical Imaging, Jiangsu Taizhou People's Hospital, Taizhou, Jiangsu Province, 225300, China.

Criteria for analysis: The latest version of ChemDIS-Mixture (v.5.0) was used for the prediction of the potential drug-drug interaction of Propranolol with Omniscan. The confidence score was adjusted to medium (0.4) shown in Fig. 1[9]. The study was conducted via a schematic method as shown in Fig. 2. The entry of the drug was added into each search bar of the

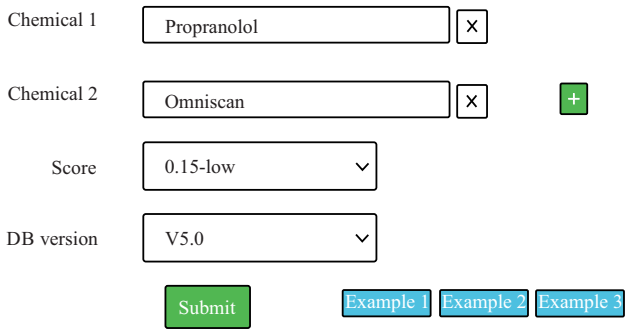

Fig. 1: Confidence score prediction of the potential drug-drug interaction of propranolol with omniscan

database, before which the parameters of the hypergeometric analysis were adjusted (Benjamini-Hochberg multiple test correction, $p<0.05$) for the analysis of GO, DO and DOLite terms as well as the proteins and molecular signalling pathways associated with the co-prescription of both drugs:

- Propranolol and Omniscan were written as the input chemical 1 and chemical 2 in the given slots
- ChemDIS-Mixture can study the interaction among four chemicals at a time. "Score" represents confidence score, which could be high, medium or low
- For this study, medium type score (i.e., 0.4) was utilized

RESULTS

ChemDIS-Mixture is an online hub of a widespread collection of data from other inter-connected databases such as PubChem. This software also has data of a vast variety of target proteins and their two and three-dimensional structures. The predictive analysis of this software thus demonstrates the outputs of the analysis through the unique effects of various target proteins, signalling pathways, GO, DO and DOLite terms, compiled altogether in Microsoft Excel® as well as Venn diagrams that denote drug-drug interactions between two drugs. The effects of the interaction of the co-administration of Propranolol and Omniscan was demonstrated via the predictive analysis in ChemDIS-Mixture (Fig. 2). Venn diagrams demonstrated the combined effects of both drugs in the form of affected proteins, GO terms, DO and DOLite terms in Fig. 3.

Proteins: Propranolol and omniscan are associated with 473 and 360 proteins, respectively. The predictive analysis characterized 134 proteins and 967 overall effects in the human body which were found to be related to the action of both drugs together in Fig. 3. The mutual interaction between both drugs was mainly associated with cytochrome P450 enzymes (CYP450). Both propranolol and omniscan are metabolized by CYP3A4 and CYP1A2, which suggests the likeliness of interference when both agents are present in the body.

GO terms: The analysis demonstrated the generation of 193 combined GO terms and individual 536 and 489 terms for Propranolol and Omniscan, respectively. Furthermore, 08 new GO terms (i.e., keratin filament binding, structural constituent of the myelin sheath, cysteine-type endopeptidase inhibitor activity involved in the apoptotic process, benzodiazepine receptor activity, oxygen transporter activity, phosphotyrosine binding, C3HC4-type RING finger domain binding and water channel activity) and 164 overall effects were also observed in the study in Table 1 and Fig. 3. Adj. PJoint values for all terms was less than 0.05. Adj. P1 values ranged between 2-4 out of 916, while Adj. P2 values were 5-22 out of 16309. Jointly, Adj. PJoint values were less than 0.05 when Propranolol and Omniscan were co-prescribed, showing the observation of the significantly large number of GO terms as compared when Propranolol was administered alone. Most of these terms were associated with skin and muscle-related ontologies.

Signalling pathways: The co-administration of Propranolol and Omniscan demonstrated 269 and 248 SMPs, while the combined SMPs for both drugs were observed to be 118. The overall new effects were found to be 188, while 04 new SMPs (Intracellular Signalling Through Prostacyclin Receptor and Prostacyclin, Excitatory Neural Signalling Through 5-HTR 6 and Serotonin, Excitatory Neural Signalling Through 5-HTR 4 and Serotonin and Excitatory Neural Signalling Through 5-HTR 7 and Serotonin) were observed in the analysis of Table 2 and Fig. 3. According to the data, gene ratio 4/171 genes and Bg ratio 8-9/1116 are involved in these signalling pathways. GeneRatio is similar to M/N where M represents the number of genes (gene set size) from the input list (the annotated distribution) that matches the signalling pathways and N is the size of all sole genes in the collection of gene sets. Similarly, BgRatio is like A/B where B indicates all genes in the database. The number of genes is specific in the database of the acquired signalling pathways terms. Here P- and Adj. The p-values for all terms were less than 0.05. It indicates that a considerable number of genes are involved in the neural signalling through 5-HTR7 and serotonin in Table 2 leading to

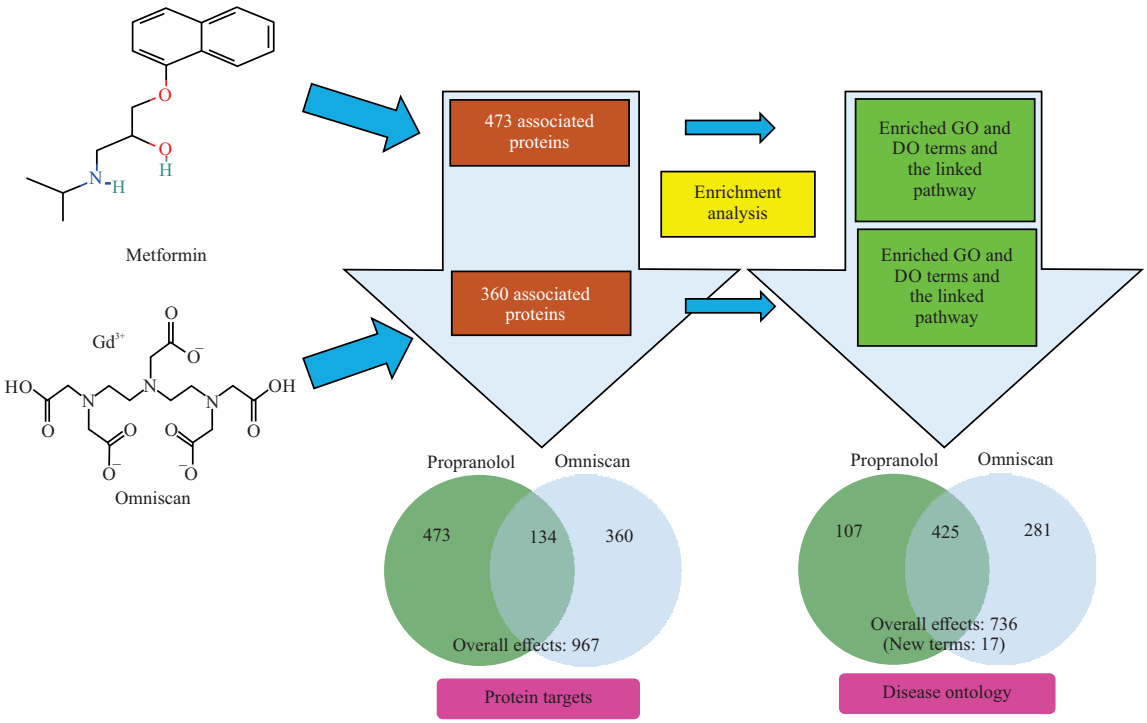

Fig. 2: Diagrammatic representation of omniscan interaction with propranolol studied through ChemDIS-mixture

Table 1: New GO terms obtained as a result of propranolol-omniscan co-prescription (unique in overall effect)

Source	ID	Description	Adj. P1	Adj. P2	Adj. Pjoint
MF	GO:1990254	Keratin filament binding	2/916	5/16309	0.02812
MF	GO:0019911	Structural constituent of myelin sheath	2/916	5/16309	0.02812
MF	GO:0043027	Cysteine-type endopeptidase inhibitor activity involved in apoptotic process	4/916	22/16309	0.03219
MF	GO:0008503	Benzodiazepine receptor activity	2/916	6/16309	0.04063
MF	GO:0005344	Oxygen transporter activity	3/916	14/16309	0.04039
MF	GO:0001784	Phosphotyrosine binding	3/916	14/16309	0.04039
MF	GO:0055131	C3HC4-type RING finger domain binding	2/916	6/16309	0.04063
MF	GO:0015250	Water channel activity	3/916	15/16309	0.04844

Table 2: New signaling pathways obtained as a result of propranolol-omniscan co-prescription (unique in overall effect)

Type	ID	Description	Gene ratio	Bg ratio	p-value	Adj. P	Genes
SMPDB	SMP00354	Intracellular signalling through prostacyclin receptor and prostacyclin	4/171	8/1116	0.02253	0.02353	GNG12, GNB1, PTGIR, ADCY2
SMPDB	SMP00312	Excitatory neural signalling through 5-HTR 6 and serotonin	4/171	9/1116	0.03579	0.03579	GNG12, GNB1, HTR6, ADCY2
SMPDB	SMP00309	Excitatory neural signalling through 5-HTR 4 and serotonin	4/171	9/1116	0.03579	0.03579	GNG12, 5-HT4, GNB1, ADCY2
SMPDB	SMP00311	Excitatory neural signalling through 5-HTR 7 and serotonin	4/171	9/1116	0.03579	0.03579	GNG12, HTR7, GNB1, ADCY2

cognitive dysfunction on concomitant administration of Propranolol-Omniscan. However, a significantly less number ($p<0.05$) of such signalling pathways is observed when Propranolol is administered alone.

DO terms: In this analysis, the shared DO terms were found to be 425, while the individual terms for Propranolol and Omniscan were observed to be 107 and 281, respectively. ChemDIS-Mixture was shown to demonstrate 736 overall effects and 17 new DO terms (prion disease, bone giant cell tumour, hyperuricemia, childhood kidney neoplasm, Huntington's disease, lymphatic system cancer, hereditary Wilms' tumour, retinitis, mature B-cell neoplasm, B-cell lymphoma, sporadic breast cancer, hepatic vascular disease, verrucous carcinoma, coccidiosis, amenorrhea, chromosomal disease and atrial heart septal defect) for the co-administration of Propranolol and Omniscan in Table 3 and Fig. 3. According to the data, gene ratio 3-17 out of 643 genes and Bg ratio 8-135 out of 8007 are involved in these disease ontologies. Here p-value and Adj. The p-values for all terms were <0.05,

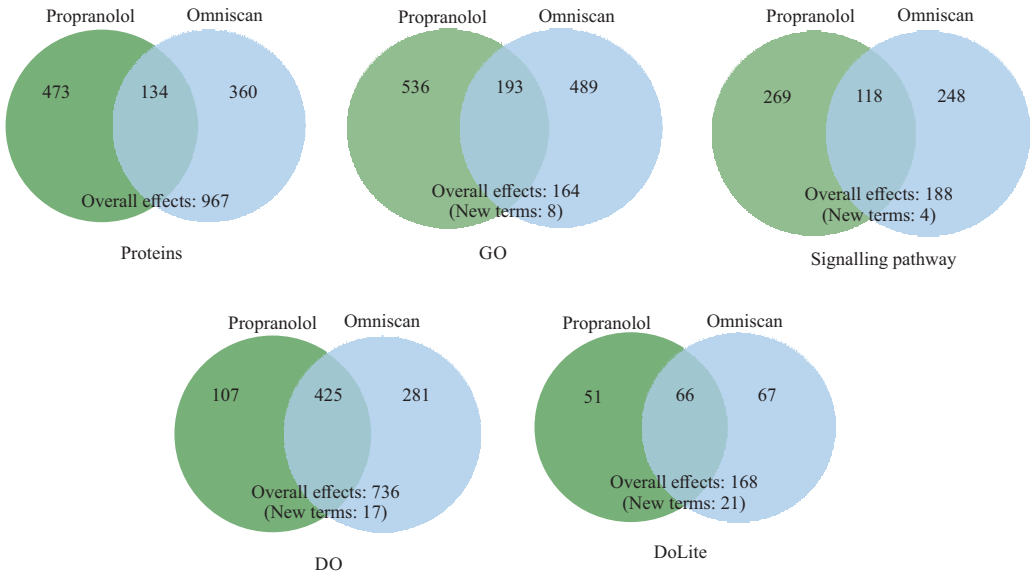

Fig. 3: Propranolol-omniscan interaction in venn diagrams based on the associated proteins, GO, pathway and DOLite terms

Table 3: New DO terms obtained as a result of propranolol-omniscan co-prescription (unique in overall effect)

DOLite ID	Description	Gene ratio	Bg ratio	p-value	Adj. P	Genes
DOID:649	Prion disease	6/643	22/8007	0.00641	0.00807	PTGS2, PRNP, CHGA, CTSD, MIWC
DOID:4305	Bone giant cell tumor	4/643	12/8007	0.01210	0.01422	TP53, CCND1, PTGS2, MET
DOID:1920	Hyperuricemia	5/643	20/8007	0.01848	0.02036	TNF, SLC22A12, ADRB3, NPPB, REN
DOID:3675	Childhood kidney neoplasm	3/643	8/8007	0.02125	0.02300	SPP1, CCND1, PIK3CA
DOID:12858	Huntington's disease	9/643	52/8007	0.02128	0.02300	HSTP, NPY, MMP2, IGF1, AKT1
DOID:0060073	Lymphatic system cancer	3/643	8/8007	0.02125	0.02300	CASP9, SCA-1, IFNG
DOID:5183	Hereditary Wilms' tumor	9/643	55/8007	0.02972	0.03125	PAX8, TP53, ABCB1, PRTN3, CYP19A1
DOID:3612	Retinitis	12/643	82/8007	0.02980	0.03128	PROM1, CCR2, RRH, GNB1, RHO
DOID:706	Mature B-cell neoplasm	5/643	23/8007	0.03287	0.03417	BCL2L1, CD117, MET, BSF-2, CCND1
DOID:707	B-cell lymphoma	5/643	23/8007	0.03287	0.03417	BCL2L1, CD117, MET, BSF-2, CCND1
DOID:8029	Sporadic breast cancer	6/643	31/8007	0.03419	0.03539	VEGFA, TP53, CYP19A1, GPX1, IFNG
DOID:272	Hepatic vascular disease	5/643	24/8007	0.03887	0.03985	CLGI, CYP2C9, F2, UTS2R, TGFB1
DOID:3737	Verrucous carcinoma	3/643	10/8007	0.04036	0.04103	TP53, CCND1, mENA
DOID:2113	Coccidiosis	3/643	10/8007	0.04036	0.04103	IFNG, TAC1, RP19
DOID:13938	Amenorrhea	3/643	10/8007	0.04036	0.04103	PRL, NPY, GNRHR
DOID:0080014	Chromosomal disease	17/643	135/8007	0.04175	0.04238	RUNX1, KISS1R, SCA-1, PROP-1, PCNA
DOID:1882	Atrial heart septal defect	4/643	17/8007	0.04225	0.04271	SLC6A4, OXTR, NPPB, F2

showing that a significant number of genes have involvement in the pathogenesis of the tabulated diseases on concomitant administration of Propranolol-Omniscan. Nonetheless, the use of Propranolol in the absence of Omniscan retrieve a non-significant number ($p<0.05$) of disease ontologies.

DOLite terms: The combined DOLite terms were found to be 66, while the individual terms were observed to be 51 and 67 for Propranolol and Omniscan, respectively. Furthermore, overall effects were found to be 168, while 21 new effects (Nephrosis, Subarachnoid haemorrhage, Autistic disorder, HIV infection, Thyroid gland disease, Fibromyalgia, Bone metastases, Bronchial hyper, reactivity, CNS metastases, Skin disease, Congenital abnormality, Melanoma, Keratosis, Mycobacterium infection, Atypical Osteomyelitis, Hyperthyroidism, Lymphoproliferative disorder, Labor, Premature, Intermediate coronary syndrome, Pervasive development disorder and Polyarthritis) were also reported shown in Table 4, Fig. 3. According to the data, gene ratio 3-24 out of 372 genes and Bg ratio 8-178 out of 4051 are involved in these Lite disease ontologies. The p-values for all terms is less than 0.05. It reveals that a significant number of genes are involved in the pathogenesis of the retrieved diseases as given in Table 4, on concomitant administration of Propranolol-Omniscan and the incidence of these diseases is relatively low ($p>0.05$) than Propranolol alone.

Table 4: New DOLites obtained as a result of propranolol-omniscan co-prescription (unique in overall effect)

DOLite ID	Description	Gene ratio	Bg ratio	p-value	Adj. P	Genes
DOLite:379	Nephrosis	6/374	20/4051	0.00752	0.01336	TNF, TFA, APOA4, OB-R, NFKB3
DOLite:509	Subarachnoid hemorrhage	4/374	11/4051	0.01395	0.02212	ALXDRD, MIWC, B2AR, ADRB1
DOLite:67	Autistic disorder	12/374	68/4051	0.02007	0.02885	Hs.22998, SLC6A4, ALXDRD, CYP21A2, MIWC
DOLite:228	HIV infection	17/374	110/4051	0.02255	0.03131	VPCAP1R, TNF, SPP1, CD34, CXCL11
DOLite:527	Thyroid gland disease	5/374	19/4051	0.02560	0.03379	hTSHR-I, crg-2, CD117, PTGS2, BCL2L1
DOLite:199	Fibromyalgia	3/374	8/4051	0.03075	0.03743	SLC6A4, IGFBP3, IGF1
DOLite:85	Bone metastases	3/374	8/4051	0.03075	0.03743	BSF-2, HEL113, IL4
DOLite:91	Bronchial hyperreactivity	3/374	8/4051	0.03075	0.03743	NPSR1, IL13, CRP
DOLite:99	CNS metastases	3/374	8/4051	0.03075	0.03743	CCL2, MMP2, DGKG
DOLite:496	Skin disease	7/374	34/4051	0.03259	0.03903	MMP9, MC1R, CTX, LIPD, bK150C2.1
DOLite:135	Congenital abnormality	24/374	178/4051	0.03560	0.04183	SCA6, SNCA, HEL70, WSS, FOXE1
DOLite:337	Melanoma	20/374	144/4051	0.04001	0.04435	TRH, CLGI, VTSIP, POMC, PLD1
DOLite:295	Keratosis	3/374	9/4051	0.04303	0.04435	TRPC1, CCND1, CTSD
DOLite:8	Mycobacterium infection, atypical	3/374	9/4051	0.04303	0.04435	SLC22A4, CCL2, IFNG
DOLite:398	Osteomyelitis	3/374	9/4051	0.04303	0.04435	RUNX1, F10, CLCN7
DOLite:265	Hyperthyroidism	3/374	9/4051	0.04303	0.04435	hTSHR-I, IGF1, IFNG
DOLite:328	Lymphoproliferative disorder	4/374	15/4051	0.04298	0.04435	BTK, CXCL9, GPR28, ETR-3
DOLite:7	Labor, premature	4/374	15/4051	0.04298	0.04435	CCL2, REN, IL1B, CRH1
DOLite:284	Intermediate coronary syndrome	3/374	9/4051	0.04303	0.04435	TNF, AGT, CRP
DOLite:427	Pervasive development disorder	4/374	15/4051	0.04298	0.04435	AVPR1, OXT, SLC6A4, MET
DOLite:434	Polyarthritis	12/374	77/4051	0.04787	0.04816	CALM1, u-PA, CYP19A1, CYP2B6, CHGA

DISCUSSION

The understanding of the possible Drug-Drug Interactions (DDIs) between two drugs is very crucial for the safe usage of both drugs as well as for the reduction in the risk of adverse drug reactions in unsuspecting patients. The average discussion of both terms underlies highlighting the pharmacokinetics and pharmacodynamics of both drugs, for deciphering which drug has an adverse reaction to the other drug and vice versa[10]. The use of gadolinium-based contrast agents and beta-blockers indicate the increased risk of hypersensitivity reactions when administered together in high-risk patients. The onset of anaphylactic reactions is reported to be more difficult to treat in those patients who have been prescribed these drugs together, although the mechanism remains to be largely unknown. If any, reactions can occur as soon as 60 min of contrast agent administration, where patients can experience several moderate hypersensitivity reactions such as edema, tachycardia, hypertension, arrhythmia and broncho-spasms. Apart from these moderate reactions, the risk of severe or fatal reactions stands at 0.005 and 0.0003%, respectively[11]. Thus, patients who have been administered contrast media and are already on a prescription of beta-blockers such as Propranolol should be strictly monitored for any kind of adverse hypersensitivity reactions. In case of anaphylaxis, attending physicians should keep in mind the attenuation to epinephrine by beta-blockers, which can be overcome by large dosages of epinephrine which also carry serious risks of hypertension, tachycardia as well as bronchospasms[12].

In this study, the predictive analysis of co-administering Propranolol with Omniscan, a gadolinium-based contrast imaging agent was investigated. The results of the study depicted 08 new GO terms, while 04 new signalling pathways, namely Intracellular signalling through prostacyclin receptor and prostacyclin (SMPID:00354), Excitatory neural signalling through 5-HTR 6 and Serotonin (SMPID:00312), Excitatory neural signalling through 5-HTR 4 and serotonin (SMPID:00309) and Excitatory neural signalling through 5-HTR 7 and serotonin (SMPID:00311). Individuals diagnosed with disorders such as anxiety and depression are often reported to react to their mental distress, which often materializes in the form of physical symptoms such as pain, gastrointestinal symptoms, fatigue as well as heart-related conditions. The action of anti-depressant drugs such as serotonin (5-HT) reuptake inhibitors (selective and dual) as well as norepinephrine (NE) reuptake inhibitors are used for their therapeutic effects against various mental disorders and their symptoms, which may be attributable to their pharmacological action exerted on serotonin and norepinephrine systems. Serotonin is a monoamine neurotransmitter whose neurons exist in the dorsal and median parts of the brain. Its release from the pre-synaptic nerve terminal is mediated by the serotonin transporter. Receptors of serotonin comprise pre-synaptic and postsynaptic receptors, which are regarded as significant mediators of the self-inhibition mechanism of serotonin neural activity. The effect of serotonin is regulated via its interaction with its receptor families, including 5-HT1-5-HT-7. Furthermore, considerable

interactions between the serotonergic and noradrenergic systems have been observed in many reports[13].

The DO term analysis yielded 17 new unique effects, such as prion disease (DOID:649), bone giant cell tumour (DOID:4305), hyperuricemia (DOID:1920), childhood kidney neoplasm (DOID:3675), Huntington's disease (DOID:12858), lymphatic system cancer (DOID:0060073), hereditary Wilms' tumour (DOID:5183), retinitis (DOID:3612), mature B-cell neoplasm (DOID:706), B-cell lymphoma (DOID:707), sporadic breast cancer (DOID:8029), hepatic vascular disease (DOID:272), verrucous carcinoma (DOID:3737), coccidiosis (DOID:2113), amenorrhea (DOID:13938), chromosomal disease (DOID:0080014), atrial heart septal defect (DOID:1882). An atrial septal defect is the second most common of all heart defects and is attributable to more than 9% of all cardiac-related problems[14]. Small atrial septal defects may arise and be diagnosed early after childbirth or in infancy, whereas large defects may cause serious heart conditions such as atrial arrhythmias, pulmonary embolisms and vascular disease as well as heart failure[15,16]. Its occurrence in childhood or adult life is commonly associated with genetic mutations of various genes such as NKX2-5, GATA4, BMP4, TBX5 and HAND1[17]. NKX2-5 serves has a crucial role in developing the atrioventricular node and its regulation[18,19]. GATA4 is also an important gene as it has been studied thoroughly in the development of heart defects and disease, including atrial septal defect[20,21]. The atrial septal defect may occur in the existing presence of congenital heart disease, where genetic mutations may prove to be pathogenic, resulting in the manifestation of disease[22]. The etiological factors for the occurrence of atrial septal defect may be dependent upon several factors which may be genetic (intrinsic) and environmental (extrinsic) in nature[23,24].

The elucidation of the possible interaction between two drugs can be carried out through ChemDIS-Mixture, an online tool that offers insight into potential DDIs between two drugs, revealing effects that may be beneficial or malignant. Nevertheless, validation of the *in silico* analysis is needed via the study findings of *in vivo* or *in vitro* research.

CONCLUSION

Propranolol is a drug that is administered for the treatment of hypertension, along with several heart conditions such as tachycardia and arrhythmia. This drug is primarily metabolized in the liver by the CYP2D6 enzyme. However, if another is administered alongside it, it may tend to cause serious effects as observed from the present analysis where the effects caused by the co-administration of Propranolol and Omniscan were investigated. Omniscan, a gadolinium-based MR imaging contrast agent can act as a CYP2D6 substrate, thereby increasing Propranolol concentrations in serum due to competitive inhibition. Therefore, it is crucial to carefully monitor the dosage and the administration of both drugs when there is a need to administer them together to the same patient.

SIGNIFICANCE STATEMENT

This study predicted the interaction of gadolinium-based MR imaging contrast agent with propranolol that can be beneficial for healthcare providers. This study will help the researchers to uncover the critical areas of drug-diagnostics interaction that many researchers were not able to explore. Thus a new theory on drug-diagnostics interaction may have arrived at the suggestion of a guideline on careful MRI scan of propranolol-treated patients.

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