Research Article

Recent activities predicted by pass software online for hypertrophic cardiomyopathy

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Abstract

Background: Hypertrophic Cardiomyopathy (HCM) is a cardiovascular disorder that is associated with major heart disorders. It is responsible for 60-80% of Heart failure cases. There is an urgent need for the discovery and development of newer drugs that could delay the progression of the disease as current pharmacotherapy offers only symptomatic liberation. **Objective**: Prediction of activity spectra of substances (PASS) is a valuable interface that should be adopted as an archetypal tool for predicting the potential anti-HCM capability of molecules and to predict the biological activity of certain phytoconstituents for their anti-HCM effects**. Materials and Methods:** Several phytoconstituents were nominated on the basis of the reported literature. The anti-HCM activities of selected phytoconstituents were predicted by engaging the canonical simplified molecular-input line-entry system obtained from PubChem.com followed by using PASS online. **Results:** Several phytoconstituents were predicted to have effects better than marketed drugs under some or the other out of the chosen areas of pharmacological mediation. On the other hand, several new paths were predicted in which the *in vitro* and *in vivo* evaluation of the phytoconstituents can be made on the basis of PASS predicted activities. **Conclusion:** PASS is an important tool for effectively showing the compounds of interest for the biological actions of interest. This helps the researchers to rationalize the research. However, PASS has its own share of limitations amidst a multitude of merits.

Keywords: Hypertrophic cardiomyopathy, phytoconstituents, Prediction of activity spectra of substances (PASS)

Introduction

Previously most common heart disorder was hypertrophic cardiomyopathy (Alcalai et al., 2008; Mogensen et al., 2004; Maron, 2002; Maroon, 2003). Which perhaps signifies tough pathophysiology and various other clinical prognoses (Semsarian et al., 2015). Until now no synthetic agent have shown proper pharmacological action due to the lateral side effect which becomes toxic at the end of the treatment. Hence only long term solution which is believed to work is surgical myectomy and implantable cardiac defibrillator. The main goal for us to use pharmacological therapy is to decrease the dynamic intra-ventricular gradient and treatment of heart failure (Ho and Seidman, 2006).

The current pharmacotherapeutic approach for hypertrophic cardiomyopathy gives symptomatic relief. There is an urgent want for the discovery and development of new drugs that ought to halt or extend the progression of the disorder through treating the underlying causes. The new drug development is a very tedious method and is related with a high probability of negative consequences in terms of pharmacological efficacy (Srinivasan et al., 2017). In such a scenario, it becomes fundamental that a device is available which ought to predict the pharmacological properties beforehand. It would allow the researchers to streamline the lookup more efficiently. Prediction of activity spectra of substances (PASS) is such a device which can predict the pharmacological homes beforehand and would help in screening pharmacological manageable leads for a particular condition (Goel et al., 2011; Parasuraman, 2011). The applicability of PASS to phytoconstituents has been exhibited in formerly investigations. The contemporary model of PASS is capable of predicting over 3750 organic effects, biochemical modes of action, specific toxicities, and metabolic phrases based on 2D constructions or canonical simplified molecular-input line-entry system (SMILES) with a imply accuracy of nearly 95%. It predicts the spectra of organic things to do for a molecule in terms of probable

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activity (Pa) and probable inactiveness (Pi) (O'mahony et al., 2013). This prediction is based on the analyses of the structure-activity relationship of the training set comprising of over 2,05,000 compounds showing over 3,750 kinds of biological activities. The present homework includes the use of PASS for a survey of the pharmacological credibility of selected phytoconstituents in treatment of HCM with respect to various disease-associated targets (Newman and Cragg, 2007).

Material and methods

On the basis of existing literature, perhaps various phytoconstituents were selected for treatment of HCM (references mentioned in Table 1). Three marketed drugs for the therapy of HCM were additionally chosen to be analyzed for prediction of biological activity spectra. (11) The canonical SMILES of these phytoconstituents and marketed drugs were acquired from PubChem (www.pubchem.ncbi.nlm.nih.gov) as in table 2. An elaborate search of existing literature was conducted to gather information referring to the antecedent reportable biological activities, both *in vitro* and *in vivo*, of those phytoconstituents (Filimonov et al., 2005). The biological activity spectra of those phytoconstituents were obtained by Canonical SMILES mistreatment PASS on-line offered from www.pharmaexpert.ru/passonline/predict.php/.

Results

Marketed drugs as well as phytoconstituents were assessed by PASS helped prediction for required HCM related pharmacotherapy. The considered intervention were; (i) Antihypercholesterolemic (including anti-hypertensive activity); (ii) Antihypolipemic; (iii) Calcium Regulator; (iv) Cholestanetriol 26-Monooxygenase Inhibitor; (v) Cholesterol Oxidase Inhibitor. The results were obtained have been presented in table 1.

Results of the study showed in figure 1 and 2 for antihypercholesterolemic and antihypolipemic activity. Figure 3 shows Calcium Regulators and in figure 4 showed the result of Pa value depicted overall pharmacological activities with respect to the marketed drug for HCM.

Discussion

PASS is an online interface which takes into deliberation a problem free enlistment at no charge. The product predicts the natural exercises of mixes by three apparatuses – canonical SMILES, MOL documents, and an inbuilt JAVA applet for illustration 2D constructions (MarvinSketch). The organic exploit spectra for a marvelous number of molecules can be estimated by PASS in a short-lived timeframe (Filimonov et al., 2014).

Table 1. PASS predicted anti-HCM activities of selected phytoconstituents and marketed synthetic drugs

Compounds	Nature	Reported Activity	Pass Predicted Activated (Pa Value/Pi Value)				
			Antihypercholesterolemic	Antihypolipemic	Calcium Regulator	Cholestanetriol 26 - Monooxygenase Inhibitor	Cholesterol Oxidase Inhibitor
Ergostero	Phytoconstutent	Anti-Hypertensive (Chang et al., 2002)	0,972/0,002	0,916/0,004	0,712/0,003	0,715/0,006	0,631/0,002
Vitexin-2-Rhamnoside	Phytoconstutent	Antihyperlepidimic (Yu et al., 2009)	#	0,408/ 0,055	0,256 /0,191	#	#
Panaquin	Phytoconstutent	Anti-Hypertensive (Seto et al., 2009)	0,219/0,099	#	#	0,430/0,025	#
Digitoxin	Phytoconstutent	Cardiotonic (Nicolai et al., 2010)	0,262/0,0725.	0,439/ 0,049	0,306/ 0,105	#	0,313 /0,019
Ginkgolides	Phytoconstutent	Antithrombotic (Fonseka et al., 2002)	#	#	#	#	#
Salvianolic Acid	Phytoconstutent	Antithrombotic (Fonseka et al., 2002)	0,449/0,029	0,608/ 0,022	0,400/ 0,041	#	#
Verapamil	Marketed Synthetic	Calcium Channel blocker	#	#	0,583/ 0,006	#	#
Furosemide	Marketed Synthetic	Diuretics	#	#	0,583/ 0,006	#	#
Metoprolol	Marketed Synthetic	Beta Blocker (Naidu, 2018	0,181/0,127	0,327/ 0,082	0,341 /0,073	#	#

#Activity not predicted by PASS

Table 2. Selected molecules/compounds for PASS prediction with respective canonical SMILES

Molecule/Compound	Canonical SMILES (obtained from PubChem)
Ergosterol	CC(C)C(C)C=CC(C)C1CCC2C1(CCC3C2=CC=C4C3(CCC(C4)O)C)C
Vitexin -2-Rhamnoside	CC1C(C(C(C(O1)OC2C(C(C(OC2C3=C(C=C(C4=C3OC(=CC4=O)C5=CC=C(C=C5)O)O)O)CO)O)O)O)O)O)O
Panaquin	C1=CC2=C(C(=C(C=C2I)I)O)N=C1
Digitoxin	CC1C(C(CC(O1)OC2C(OC(CC2O)OC3C(OC(CC3O)OC4CCC5(C(C4)CCC6C5CCC7(C6(CCC7C8=CC(=O)OC8)O)C)C)C)O)O)O
Ginkgolides	CC1C(=O)OC2C1(C34C(=O)OC5C3(C2O)C6(C(C5)C(C)(C)C)C(C(=O)OC6O4)O)O
Salvianolic Acid	C1=CC(=C(C=C1CC(C(=O)O)OC(=O)C=CC2=C(C(=C(C=C2)O)O)C=CC3=CC(=C(C=C3)O)O)O)O
Verapamil	CC(C)C(CCCN(C)CCC1=CC(=C(C=C1)OC)OC)(C#N)C2=CC(=C(C=C2)OC)OC
Furosemide	C1=COC(=C1)C NC2=CC(=C(C=C2C(=O)O)S(=O)(=O)N)Cl
Metoprolol	CC(C)NCC(COC1=CC=C(C=C1)CCOC)O

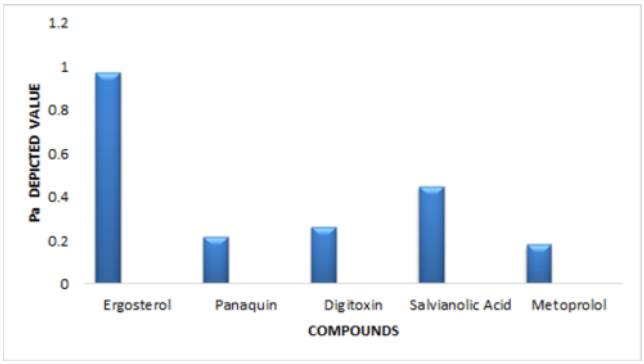

Figure 1. Relative Antihypercholesterolemic activity of selected compounds

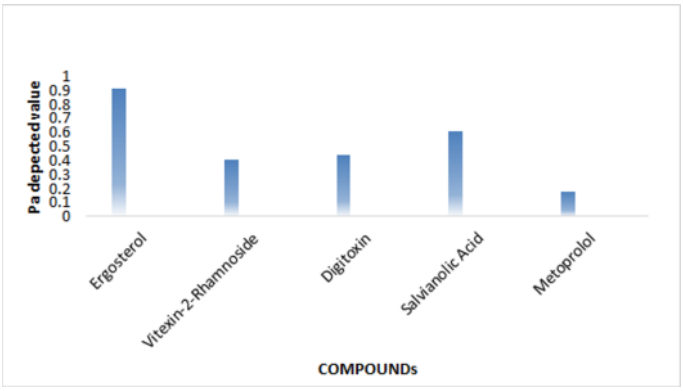

Figure 2. Relative Anti Antihypolipemic activity of selected compounds

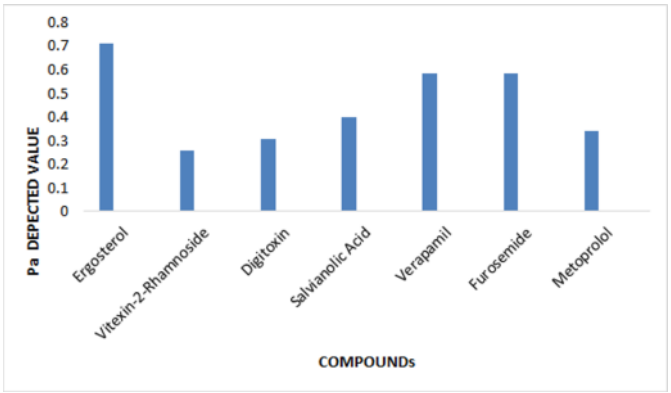

Figure 3. Relative Calcium Regulator activity of selected compounds

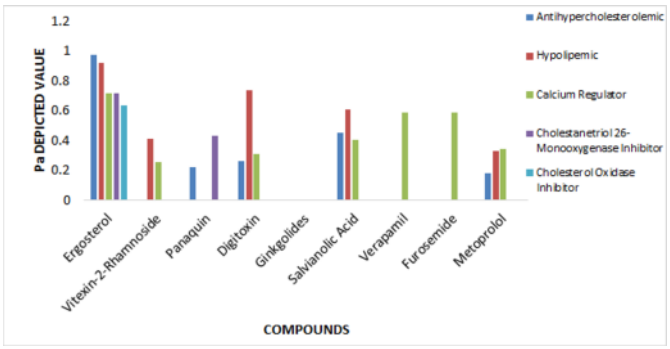

Figure 4. An impression of the prediction of activity spectra of substances predicted probable activity values for selected compounds under the 5 areas of pharmacological medications for treatment of HCM

The marketed drug was analysed with resected to the natural phytoconstituents which were reported in the literature for anti-HCM activity by PASS prediction. Further, the analysis was done under five area of the Pharmacotherapeutic Avenue, which at the end gave the results in terms of Pa value reported in table 1 and graphically represented in figure 4.

While selected phytoconstituents did not exhibit Anti-HCM, which perhaps could be co-related with the selected pharmacotherapeutic intervention, hence resulted phytoconstituents were Ginkgolides were one of them. Where Ergosterol shows more Pa value resulted most optimum for Anti-HCM activity which has shown all the activity by PASS software. Beforehand if we have to take a look the comparison of both marketed and phytoconstituents intervention, reported phytoconstituents have shown better-depected activity as compared to the marketed drug which has only been proven to show certain action mention in Table 1. With severe side effects. But this cannot be neglected that metoprolol has shown certain accepted activities as well.

PASS benefits in picking and optimizing the compounds, based on the structure of predicted target site of attention for computer-aided drug design and enables the pharmacist to speed up the process. It is a very beneficial instrument for skimpy novel modes of action of existing molecules. It helps in finding new lead compounds which can be further optimized. The chief benefit is the software's capability to predict a wide array of organic activities in a nominal amount of time.

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