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Prediction of Biological Activity Spectra of *Alpinia* Phytochemicals by an *In Silicon* Study

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Abstract

Bioinformatics derives knowledge from computer analysis of biological data. Biologically active compounds have both pharmaceutical and toxic effect in the organisms. PASS software is used to estimate general efficacy and safety of the molecules. PASS simultaneously predicts several hundreds of biological activities of chemical compounds. In the present study phytochemicals reported from two species of Alpinia were subjected to in silicon evaluation using PASS software. The average accuracy of prediction is about 80%. The methods, results and significance of this in silicon study is discussed.

INTRODUCTION

Medicinal plants have been used for years in daily life to treat human diseases all over the world. Different extracts from medicinal plants were tested and some natural products that produce definite biological action were approved as drugs. The secondary metabolites, such as alkaloids, flavonoids, lignins, terpenoids, steroids, glycosides, coumarins, and phenolic molecules in plant materials possess these curative effect [7]. Many medicinally important compounds are extracted from the plant species of family Zingiberaceae. (ginger family). Of these several bioactivies have been identified in the genus *Alpinia*. *Alpinia* is the largest genus in the ginger family, with about 230 species. A number of those are commonly grown for their flowers, and others are used as spices [2]. In the present study our effort has been made to use bioinformatics tool for predicting activity of phytochemicals present in the species of *Alpinia* (fig 1a-d). Bioinformatics is a multidisciplinary field that develops methods and software tools for understanding biological data. Computational techniques developed by researchers in bioinformatics have been beneficial to scientists and entrepreneurs in other fields also [4]. The primary goal of bioinformatics is to increase the understanding of biological processes. Bioinformatics tools are used for the *in silicon* study of active principles of medicinal plants. PASS (Prediction of Activity Spectra for Substances) tool interprets the biological activity spectra using 2D structure of molecules.

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MATERIAL AND METHODS

Prediction of Activity Spectra for Substances (PASS) is hosted by Orechovich Institute of Biomedical Chemistry under the aegis of the Russian Foundation of Basic Research. The web-based application predicts the biological activity spectrum of a compound based on its structure. It works on the principle that the biological activity of a compound equates to its structure. PASS web tool can freely display the predicted activity of a

Figure 1

(a) ***Alpinia calcarata*** **- Rhizome with roots**

(b) ***Alpinia calcarata*** **-Twig with inflorescence**

(c) ***Alpinia galanga*** **- Habit**

(d) ***Alpinia galanga*** **- Rhizome with roots**

molecule at various threshold levels. Activity of the molecule is predicted by comparing the structure of new compound with structure of well-known biological active substrate existing in the database. Accuracy of PASS prediction depends on comprehensive information about biological activity spectrum for each compound available in PASS training set, and therefore, the estimate of biological activity is more accurate [5]. Fig. 2 provides a flow sheet of instructions to use PASS.

Fig 2: Flow Sheet for using PASS

Enter PASS website www.pharmaexpert.ru

↓

PASS Homepage is opened

↓

Click registration

↓

Fill up the registration form and click submit

↓

PASS software Homepage is opened

(www.pharmaexpert.ru/passonline/predict.php)

↓

Enter the User name and password and click ok

↓

Click Predict New compound

↓

New applet software is opened

↓

Draw the structure of the compound using Marvin sketch and click predict

↓

Activities of the compound will be displayed

In the present investigation, the important active principles (Table 1) from *Alpinia calcarata* and *Alpinia galanga* were subjected to *in silicon* analysis to get their activity spectra.

Table 1 – Phytochemicals subjected to PASS

S. No.	Name of the compound	*Alpinia calcarata*	*Alpinia galanga*
1.	1-Acetoxy chavicol acetate	–	Rhizome, Seed
2.	1-Acetoxy euginol acetate	–	Rhizome, Seed
3.	β-Bisapoline	_	Leaf
4.	Borneol	Rhizome, Root, Leaf	Rhizome, Leaf
5	Camphene	Rhizome,Root, Leaf	Rhizome
6	Camphor	Rhizome, Stem	Rhizome
7	Carotol	Root, Rhizome, Stem	Flower
8	β- Caryophyllene	Rhizome, Root	Leaf, Flower
9	1, 8- Cineol	Rhizome, Root, Leaf	Flower
10	α- Frenchyl acetate	Rhizome, Leaf	Rhizome
11	Galangin	__	Rhizome
12	7-Heptadecan	__	Seed
13	α-Humulene	__	Rhizome
14	p- Hydroxy benzaldehyde	––	Rhizome
15	p-Hydroxy cinnamaldehyde	––	Rhizome
16	di-p-Hydroxy cis styryl methane	––	Rhizome
17	Kaemferol	__	Rhizome
18	Limonene	Rhizome, Flower, Leaf	Flower
19	Linalool	Linalool	Flower
20	Methyl cinnamate	Rhizome, Root, Flower	Rhizome, Leaf
21	Methyleuginol	__	Flower
22	Pentadecan	__	Seed
23	α-Pinene	Rhizome, Leaf, Flower	Rhizome, Leaf, Flower
24	β-Pinene	Rhizome	Rhizome
25	Protocatchuic acid	Root, Leaf	__
26	β-Phyllandrene	__	Flower
27	Quercetin	Root	Rhizome
28	β-Selinine	__	Flower
29	Syringic acid	__	Rhizome
30	α-Terpenol	Rhizome, Root, Leaf	Rhizome, Flower
31	4-Terpenol	Rhizome, Root, Leaf	Rhizome
32	Trans -p- coumaryl alcohol	––	Rhizome
33	Trans -p- hydroxyl cinnamaldehyde	––	Rhizome
34	Vanillic acid	Root, Leaf	__

RESULTS AND DISCUSSION

The activity spectra of 34 phytochemicals of *Alpinia galanga* and *A. calcarata* were obtained using PASS software. Due to the paucity of space only the pinnacle five activities of the compounds are listed below. For compound 11, Galangin present in *Alpinia galanga,* the list of activities having more than 90% efficiency is provided. Fig.3 shows the PASS Homepage.

Activity Spectra of the phytochemicals

Compound 1 - 1-Acetoxy chavicol acetate

0,983	0,002	Interleukin 4 antagonist
0,909	0,004	Gluconate 2-dehydrogenase (acceptor) inhibitor
0,795	0,035	Aspulvinone dimethylallyl-transferase inhibitor
0,776	0,026	Mucomembranous protector
0,710	0,003	Nitric oxide antagonist

Compound 2 - **1-Acetoxy euginol acetate**

0,867	0,005	Apoptosis agonist
0,853	0,004	Anesthetic general
0,818	0,003	Carminative
0,812	0,016	Antieczematic
0,767	0,009	Antiinflammatory

Compound 3 **- β-bisapoline**

0,859	0,009	Antieczematic
0,816	0,001	Retinol dehydrogenase inhibitor
0,813	0,004	Carminative
0,815	0,015	Mucomembranous protector
0,783	0,004	Prenyl-diphosphatase inhibitor

Compound 4 **- Borneol**

0,962	0,002	Testosterone 17beta-dehydrogenase (NADP+) inhibitor
0,954	0,002	Acylcarnitine hydrolase inhibitor
0,946	0,002	Alkylacetylglycerophosph-atase inhibitor
0,947	0,003	Alkenylglycerophosph-ocholine hydrolase inhibitor
0,942	0,003	CYP2J substrate

Compound No 5 - **Camphene**

0,977	0,001	Cardiovascular analeptic
0,940	0,002	Vasoprotector
0,936	0,004	Testosterone 17beta-dehydrogenase (NADP+) inhibitor
0,935	0,004	Respiratory analeptic
0,906	0,004	CYP2J substrate

Compound 6 **- Camphor**

0,977	0,001	Cardiovascular analeptic
0,940	0,002	Vasoprotector
0,936	0,004	Testosterone 17beta-dehydrogenase (NADP+) inhibitor
0,935	0,004	Respiratory analeptic
0,906	0,004	CYP2J substrate

Compound 7 **- Carotol**

0,986	0,001	Chlordecone reductase inhibitor
0,973	0,002	Membrane integrity agonist
0,971	0,001	2-Dehydropantoate 2-reductase inhibitor
0,968	0,001	Aryl-alcohol dehydrogenase (NADP+) inhibitor
0,969	0,002	HIF1A expression inhibitor

Compound 8 **- β- caryophyllene**

0,859	0,009	Antieczematic
0,847	0,009	Mucomembranous protector

0,831	0,014	CYP2J substrate
0,744	0,023	CYP2J2 substrate
0,725	0,013	Oxidoreductase inhibitor

Compound 9 - **1, 8- Cineol**

0,986	0,001	Chlordecone reductase inhibitor
0,973	0,002	Membrane integrity agonist
0,971	0,001	2-Dehydropantoate 2-reductase inhibitor
0,968	0,001	Aryl-alcohol dehydrogenase (NADP+) inhibitor
0,969	0,002	HIF1A expression inhibitor

Compound 10 - **α- frencyl acetate**

0,897	0,004	Acylcarnitine hydrolase inhibitor
0,898	0,006	Testosterone 17beta-dehydrogenase (NADP+) inhibitor
0,891	0,005	CYP2J substrate
0,871	0,007	Antiseborrheic
0,843	0,008	CYP2J2 substrate

Compound 11 **- Galangin**

0,980	0,001	Chlordecone reductase inhibitor
0,973	0,002	Membrane integrity agonist
0,968	0,002	HIF1A expression inhibitor
0,966	0,001	2-Dehydropantoate 2-reductase inhibitor
0,962	0,001	Aryl-alcohol dehydrogenase (NADP+) inhibitor
0,960	0,001	Kinase inhibitor
0,957	0,001	P-benzoquinone reductase (NADPH) inhibitor
0,957	0,002	Membrane permeability inhibitor
0,955	0,001	Peroxidase inhibitor
0,951	0,001	Quercetin 2,3-dioxygenase inhibitor
0,950	0,001	CYP1A inducer
0,944	0,002	HMOX1 expression enhancer
0,942	0,001	NADPH-ferrihemoprotein reductase inhibitor
0,944	0,004	CYP1A substrate
0,940	0,001	Antimutagenic
0,936	0,003	CYP1A1 substrate
0,931	0,001	Glycerol dehydrogenase (NADP+) inhibitor
0,929	0,001	CYP1A1 inducer
0,928	0,002	Alcohol dehydrogenase (NADP+) inhibitor
0,929	0,004	TP53 expression enhancer
0,925	0,001	2-Enoate reductase inhibitor
0,924	0,001	2-Dehydropantolactone reductase (A-specific) inhibitor
0,923	0,002	UGT1A6 substrate
0,924	0,007	CYP2C12 substrate
0,917	0,001	Cystathionine beta-synthase inhibitor
0,918	0,004	Ubiquinol-cytochrome-c reductase inhibitor
0,915	0,004	CYP1A2 substrate
0,913	0,002	UGT1A9 substrate
0,904	0,002	MAP kinase stimulant
0,903	0,001	Beta-carotene 15,15'-monooxygenase inhibitor
0,902	0,002	NADPH oxidase inhibitor
0,901	0,002	Histidine kinase inhibitor
0,899	0,004	Anaphylatoxin receptor antagonist

Compound 12 **- 7-heptadecan**

0,954	0,002	Sugar-phosphatase inhibitor
0,950	0,002	Acrocylindropepsin inhibitor
0,950	0,002	Chymosin inhibitor
0,950	0,002	Saccharopepsin inhibitor
0,942	0,002	Acylcarnitine hydrolase inhibitor

Compound 13 - **α-humulene**

0,900	0,005	CYP2J substrate
0,898	0,003	Phosphatidylcholine-retinol O-acyltransferase inhibitor
0,886	0,003	All-trans-retinyl-palmitate hydrolase inhibitor
0,856	0,009	Antieczematic
0,839	0,005	Apoptosis agonist

Compound 14 **- p- hydroxy benzaldehyde**

0,950	0,002	Feruloyl esterase inhibitor
0,946	0,004	Membrane integrity agonist
0,933	0,001	Vanillyl-alcohol oxidase inhibitor
0,908	0,005	Ubiquinol-cytochrome-c reductase inhibitor
0,909	0,006	Aspulvinone dimethylallyltransferase inhibitor

Compound 15 **- p-hydroxy cinnamaldehyde**

0,957	0,002	Feruloyl esterase inhibitor
0,922	0,004	CYP2J substrate
0,912	0,003	GST A substrate
0,906	0,000	Aldehyde dehydrogenase 1 substrate
0,906	0,001	Aldehyde dehydrogenase 2 substrate

Compound16 **- Di-p-hydroxy cis styryl methane**

0,931	0,005	Membrane integrity agonist
0,923	0,002	JAK2 expression inhibitor
0,923	0,005	Aspulvinone dimethylallyltransferase inhibitor
0,917	0,003	Feruloyl esterase inhibitor
0,896	0,005	CYP2J substrate

Compound 17 **- Kaemferol**

0,983	0,001	Chlordecone reductase inhibitor
0,974	0,002	Membrane integrity agonist
0,969	0,002	HIF1A expression inhibitor
0,965	0,001	2-Dehydropantoate 2-reductase inhibitor
0,961	0,001	Aryl-alcohol dehydrogenase (NADP+) inhibitor

Compound 18 **– Limonene**

0,961	0,001	Carminative
0,960	0,003	CYP2B1 substrate
0,934	0,000	Retinol dehydrogenase inhibitor
0,908	0,004	CYP2B substrate
0,896	0,005	Antieczematic

Compound 19 - **Linalool**

0,978	0,002	Mucomembranous protector
0,910	0,003	Cell adhesion molecule inhibitor
0,896	0,009	Aspulvinone dimethylallyltransferase inhibitor
0,868	0,003	Fatty-acyl-CoA synthase inhibitor
0,860	0,007	Beta-adrenergic receptor kinase inhibitor

Compound 20 **- Methyl cinnamate**

0,939	0,004	Membrane integrity agonist
0,938	0,003	Feruloyl esterase inhibitor
0,867	0,004	Phosphatidylcholine-retinol O-acyltransferase inhibitor

0,873	0,011	Phobic disorders treatment
0,862	0,004	Fusarinine-C ornithinesterase inhibitor

Compound 21 - **Methyleuginol**

0,950	0,001	Carminative
0,923	0,005	Aspulvinone dimethylallyl-transferase inhibitor
0,911	0,001	Steroid N-acetylglucosaminyl-transferase inhibitor
0,893	0,005	Antieczematic
0,851	0,005	CYP2A substrate

Compound 22 - **Pentadecan**

0,954	0,002	Sugar-phosphatase inhibitor
0,950	0,002	Acrocylindropepsin inhibitor
0,950	0,002	Chymosin inhibitor
0,950	0,002	Saccharopepsin inhibitor
0,942	0,002	Acylcarnitine hydrolase inhibitor

Compound 23 - **α-pinene**

0,863	0,012	Testosterone 17beta-dehydrogenase (NADP+) inhibitor
0,844	0,012	CYP2J substrate
0,821	0,004	Cardiovascular analeptic
0,792	0,009	5-O-(4-coumaroyl)-D-quinate 3'-monooxygenase inhibitor
0,780	0,001	Alpha-pinene-oxide decyclase inhibitor

Compound 24 **- β-pinene**

0,902	0,005	Antieczematic
0,857	0,013	Testosterone 17beta-dehydrogenase (NADP+) inhibitor
0,846	0,011	CYP2J substrate
0,758	0,005	Cardiovascular analeptic
0,753	0,002	Prostaglandin E1 antagonist

Compound 25 **- Protocatchuic acid**

0,963	0,002	Chlordecone reductase inhibitor
0,959	0,001	Dehydro-L-gulonate decarboxylase inhibitor
0,957	0,002	Arylacetonitrilase inhibitor
0,954	0,001	Glutathione thiolesterase inhibitor
0,952	0,001	Alkane 1-monooxygenase inhibitor

Compound 26 **- β-phyllandrene**

0,916	0,004	Antieczematic
0,883	0,002	Carminative
0,830	0,014	Alkenylglycerophos-phocholine hydrolase inhibitor
0,817	0,001	Testosterone agonist
0,799	0,012	Antineoplastic

Compound 27 **- Quercetin**

0,986	0,001	Chlordecone reductase inhibitor
0,973	0,002	Membrane integrity agonist
0,971	0,001	2-Dehydropantoate 2-reductase inhibitor
0,968	0,001	Aryl-alcohol dehydrogenase (NADP+) inhibitor
0,969	0,002	HIF1A expression inhibitor

Compound 28 **- β-selinine**

0,914	0,005	Antineoplastic
0,874	0,007	Antieczematic
0,857	0,001	Retinol dehydrogenase inhibitor
0,858	0,004	Dermatologic
0,856	0,006	CYP2C substrate

Compound 29 **- Syringic acid**

0,949	0,002	Chlordecone reductase

		inhibitor
0,929	0,004	Aspulvinone dimethylallyl-transferase inhibitor
0,925	0,004	Ubiquinol-cytochrome-c reductase inhibitor
0,910	0,002	4-Methoxybenzoate monooxygenase (O-demethylating) inhibitor
0,909	0,002	2-Hydroxyquinoline 8-monooxygenase inhibitor

Compound 30 **- α-terpenol**

0,859	0,009	Antieczematic
0,816	0,001	Retinol dehydrogenase inhibitor
0,813	0,004	Carminative
0,815	0,015	Mucomembranous protector
0,783	0,004	Prenyl-diphosphatase inhibitor

Compound 31 - **4-terpenol**

0,871	0,019	CYP2C12 substrate
0,838	0,011	Antieczematic
0,829	0,003	Carminative
0,842	0,019	Ubiquinol-cytochrome-c reductase inhibitor
0,812	0,022	Testosterone 17beta-dehydrogenase (NADP+) inhibitor

Compound 32 **- Trans -p- coumaryl alcohol**

0,950	0,002	Feruloyl esterase inhibitor
0,946	0,004	Membrane integrity agonist
0,933	0,001	Vanillyl-alcohol oxidase inhibitor
0,908	0,005	Ubiquinol-cytochrome-c reductase inhibitor
0,909	0,006	Aspulvinone dimethylallyl-transferase inhibitor

Compound 33-**Trans -p- hydroxyl cinnamaldehyde**

0,957	0,002	Feruloyl esterase inhibitor
0,922	0,004	CYP2J substrate
0,912	0,003	GST A substrate
0,906	0,000	Aldehyde dehydrogenase 1 substrate
0,906	0,001	Aldehyde dehydrogenase 2 substrate

Compound 34 - **Vanillic acid**

0,964	0,002	Chlordecone reductase inhibitor
0,937	0,003	Aldehyde oxidase inhibitor
0,931	0,003	Feruloyl esterase inhibitor
0,932	0,004	Aspulvinone dimethylallyltransferase inhibitor
0,924	0,002	2-Hydroxyquinoline 8-monooxygenase inhibitor

The findings correlate with the *in vitro* and *in vivo* studies of the biological spectra of the active principles reported in the literature. The efficacy of the activities of the compounds and also the negative impacts can be estimated using PASS software. This will help to design new drugs and to identify the medicinal uses of the plant [3]. The activities related with metabolic, disorders can also be corrected by these phytochemicals. In medical field, more drugs may be available for a particular disease [1]. One can select the best one by subjecting the structure of all the compounds to PASS software.

Alpinia calcarata rhizome is also adulterated with *Acorus calamus* due to its morphological similarity and also used as a substitute for *Alpinia galanga* for the presence of similar active principles. The PASS spectra can also be used to check the purity of the products in terms of their chemical profiles & finger prints. The significance of *in silicon* study is easy to perform, ecofriendly, also saves time and energy.

PASS HOMEPAGE

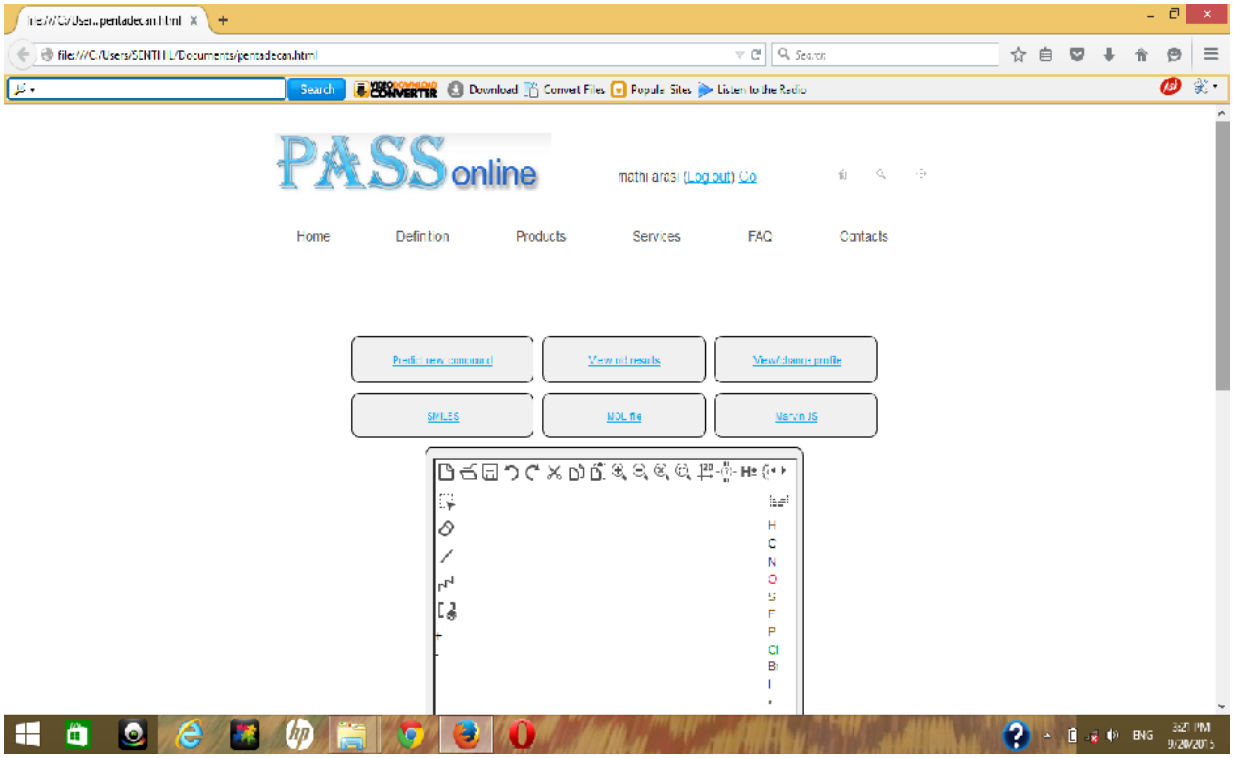

Fig1. PASS Home Page.

CONCLUSION

The results of the *in silicon* studies of phytochemical actvities are 80% reliable. After knowing the activities of the compounds, it may be validated by *in vivo*, *in vitro* screening studies and clinical trials. New actions of the drug can also be discovered through computer aided prediction.

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