PASS: Prediction of Activity Spectra for Biologically Active Constituent of Polygodial (A Drimane Type of Dialdehyde Sesquiterpene)

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Summary

The computer system PASS provides simultaneous prediction of several hundreds of biological activity types for any drug- like compound. In this study, polygodial has 25 different chemical descriptors including one new descriptor and predicted biological activity spectrum contains 114 types of activities were using the PASS software. Conclusion of report the more interesting of several activities such as antiviral, antiinflammatory, antineoplastic and antiviral (Influenza) were predicted in this compound.

Keywords: PASS software; Polygodial; *Polygonum hydropiper*; antiinflammatory activity

Introduction

PASS is an effective tool for predicting drug- like properties. The biological activity spectra predicted by PASS software is capable of distinguishing pharmaceutical effects, side effects, reaction mechanism of biochemistry, genetic mutation, carcinogenesis, toxicity, effect on fetus and other biological activities of chemicals compounds [1]. Pass prediction is based on the analysis of structure- activity relationships of the training set including a great number of non-congeneric compounds with different biological activities. The characteristics of about 4,500 compounds with different functional groups are stored in the memory of this software, with an accuracy of prediction for thousands of chemicals compounds approximately 85 % [1]. PASS once trained is able to predict many types of activity for new substance. Recently, Prediction of *Activity Spectra* for four flavoniod constituents viz; pinostrobin, pinocembrin, cardamonin and alpinetin were predicted [2].

Polygodial, a drimane type dialdehyde sesquiterpene, was isolated from *Polygonum hydropiper* L [3]. This compound presents, among other properties, insect antifeedant, antibiotic and antifungal activities. According to McCallion *et al*., (1982) reported the highly activity against *Candida albicans* [4], and this compound that displays an anti-hyperalgestic property in models of inflammatory and neurogenic pain [5]. A specific server has been generated which predicts the possibility of a drug to be active against a target based on the physico-chemical methods using comparisons and several algorithms. It is observed that the approach, used in PASS, may be applied to other biological activities [6-7].

Materials and Methods

Fig.1 Polygodial, a drimane type dialdehyde sesquiterpene, was first isolated from *Polygonum hydropiper* L. [3]. The Internet version of the program, PASS Inet predicted active constituents of Polygodial were send via the Internet a standard Molfile, which was prepared with the ISIS/Draw chemical editor website on http://www.mdli.com. The biological activity spectrum of PASS was designed and prediction was made with the comparison from the source data available http://195.178.207.233/PASS/socket1.php. Biological activity spectrum of a compound presents exhibit its activity despite the difference in essential conditions of its experimental determination.

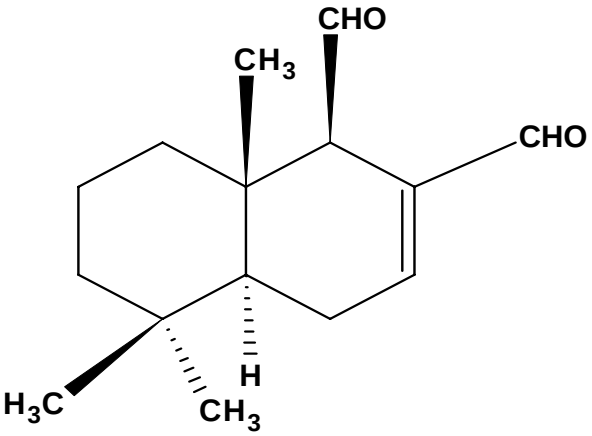

Fig.1: Polygodial

Results and Discussion

The present study of biological activity spectrum of PASS designed and prediction of active principle of Polygodial was first isolated from *Polygonum hydropiper* L.[3]. Analysis of the NMR spectral data of this compound was published literature [8-9]. Physical data of Polygodial $[\alpha]_D^{25}$= -27^o (CH_2CL_2,c=0.1). ^{13}C NMR (Brucker, 100 MHz, $CDCL_3$) :39.61(t,C1); 39.61(t,C2):41.82(t,C3); 29.71(s,C4); 49.03(d,C5); 25.24 (t,C6); 153.96 (d,C7); 138.48(s,C8); 60.36 (d,C9); 36.93(s,C10); 201.89(d,C11); 193.21 (d,C12); 21.96(q,C13); 33.14(q,C14); 15.29;(q,C15). ^{1}H NMR (Brucker,400MHz, $CDCL_3$): 9.54(d,J=4.4,H11); 9.46(s,H12); 7.13(m,H7); 2.83(m,H9); 2.51(m,H6); 2.32(m,H6); 1.85(m,H1); 0.96(s,CH_3); 0.95(s,CH_3); 0.92(s,CH_3). As shown in figure -2, polygodial has 25 different chemical descriptors including one new descriptor (which is absent in the PASS Inet training set) and predicted biological activity spectrum contain 114 types of activities. The results showed that polygodial could possess several biological activities including Antiviral (through the server http://195.178.207.233/PASS/socket1.php,(Table-1). More interestingly, this compound showed Antiinflammatory, Antineoplastic and Antiviral (Influenza). Looking through the predicted biological activity spectrum of polygodial one cannot help noticing that on the one hand Polygodial is a transforming growth factor beta 1 agonist, but on the other hand it is a transforming growth factor beta 1 agonist. Such ambiguities indicate that the active principle does interact with transforming growth factor beta 1 agonist; however, the mechanism of its instrinct action cannot be elucidated by the PASS program.

Conclusion

The application of computerized system PASS in the process of new drugs R&D in many cases provides the possibilities to select compounds with desirable spectra of therapeutic effects and minimum side actions prior to experimental testing or even synthesis. The results showed that polygodial could possess several pharmacological activities such as antiviral, antiinflammatory, antineoplastic and antiviral (Influenza). The system can not be predict all the possible properties for every compound because its possibilities limited in particular by using an appropriate training set and list of activities. But PASS is open to further development oriented in specific field of interest of any researcher or company.

Table-1: List of biological activities predicted by PASS version 4.2

No	Pa	Pi	Activity
1	0,862	0,000	Cholesterol ester transfer protein antagonist
2	0,813	0,037	Phosphatase inhibitor
3	0,767	0,027	Cardiovascular analeptic
4	0,705	0,001	Transforming growth factor beta 1 agonist
5	0,699	0,012	Antipruritic
6	0,685	0,019	Nerve growth factor agonist
7	0,663	0,013	Antipruritic, allergic
8	0,663	0,021	Neurotrophic factor enhancer
9	0,640	0,013	Dermatologic
10	0,618	0,014	Antipsoriatic
11	0,622	0,023	Carminative
12	0,580	0,022	Menopausal disorders treatment
13	0,677	0,147	Antiseborrheic
14	0,541	0,024	Gynecological disorders treatment
15	0,525	0,012	Retinol dehydrogenase inhibitor
16	0,532	0,039	Immunosuppressant
17	0,515	0,026	Microtubule formation stimulant
18	0,495	0,015	Cholesterol oxidase inhibitor
19	0,536	0,066	Tocolytic
20	0,521	0,056	CYP2B5 substrate
21	0,556	0,098	Oxidoreductase inhibitor
22	0,575	0,118	Ecdysone 20-monooxygenase inhibitor
23	0,481	0,058	Ovulation inhibitor
24	0,511	0,090	Antidyskinetic
25	0,465	0,050	DELTA14-sterol reductase inhibitor
26	0,479	0,068	Antineoplastic
27	0,487	0,078	Neurotransmitter uptake inhibitor
28	0,432	0,029	DNA ligase (ATP) inhibitor
29	0,421	0,020	Contraceptive female
30	0,429	0,030	Contraceptive
31	0,483	0,086	CYP2A2 substrate
32	0,465	0,072	**Antiinflammatory**
33	0,390	0,004	Retinoic acid receptor antagonist
34	0,394	0,020	Retinyl-palmitate esterase inhibitor
35	0,423	0,054	Skin diseases treatment
36	0,475	0,109	Apoptosis agonist
37	0,474	0,110	Cholesterol synthesis inhibitor
38	0,445	0,086	Neurotrophic factor
39	0,426	0,072	Peptidoglycan glycosyltransferase inhibitor
40	0,479	0,129	Dopamine D4 agonist
41	0,441	0,094	GABA receptor antagonist
42	0,352	0,008	Alpha-pinene-oxide decyclase inhibitor
43	0,360	0,017	Retinal dehydrogenase inhibitor
44	0,356	0,014	Hair growth stimulant
45	0,527	0,188	Hematotoxic
46	0,416	0,077	ATPase inhibitor
47	0,395	0,069	CYP4A11 substrate

48	0,373	0,047	Reductant
49	0,394	0,070	Chemopreventive
50	0,346	0,023	Growth factor agonist
51	0,414	0,099	H^+transporting two-sector ATPase inhibitor
52	0,334	0,021	Keratoses actinic (solar) treatment
53	0,324	0,011	Protein synthesis stimulant
54	0,347	0,036	Myc inhibitor
55	0,328	0,020	Antiacne
56	0,376	0,072	Emetic
57	0,313	0,015	11-Cis-retinyl-palmitate hydrolase inhibitor
58	0,441	0,147	CYP2A1 substrate
59	0,406	0,117	Steroid N-acetyl glucosaminyl transferase inhibitor
60	0,370	0,088	CYP2C11 substrate
61	0,315	0,033	Keratolytic
62	0,433	0,151	Lysase inhibitor
63	0,392	0,110	CYP2B11 substrate
64	0,315	0,037	Antichol elithogenic
65	0,461	0,184	Muco membranous protector
66	0,445	0,169	Beta-adrenergic-receptor kinase inhibitor
67	0,401	0,126	Carbonyl reductase (NADPH) inhibitor
68	0,320	0,048	Gestagen antagonist
69	0,328	0,057	Contraceptive male
70	0,308	0,041	Choloylglycine hydrolase inhibitor
71	0,338	0,073	Respiratory analeptic
72	0,379	0,116	Antiinflammatory, ophthalmic
73	0,377	0,119	Cholesterol antagonist
74	0,392	0,136	N-(long-chain-acyl)ethanolamine deacylase inhibitor
75	0,344	0,095	CYP2A5 substrate
76	0,314	0,064	CYP2A11 substrate
77	0,339	0,090	Indanol dehydrogenase inhibitor
78	0,331	0,083	Ligase inhibitor
79	0,376	0,130	Bilirubin oxidase inhibitor
80	0,341	0,095	Protein-*S*-isoprenylcysteine O-methyltransferase inhibitor
81	0,307	0,061	Antipruritic, non-allergic
82	0,341	0,099	**Antiviral (Influenza)**
83	0,373	0,132	Septic shock treatment
84	0,337	0,103	Analeptic
85	0,321	0,095	Antineoplastic (multiple myeloma)
86	0,366	0,148	Gonadotropin antagonist
87	0,331	0,114	Cholestanetriol 26-monooxygenase inhibitor
88	0,423	0,229	NADPH oxidase inhibitor
89	0,356	0,170	Trans-penta prenyl transtransferase inhibitor
90	0,402	0,225	General pump inhibitor
91	0,353	0,179	Urease inhibitor
92	0,333	0,161	Phospholipase C inhibitor
93	0,327	0,165	P-benzoquinone reductase (NADPH) inhibitor
94	0,334	0,179	Toxic
95	0,360	0,208	HDL-cholesterol increasing
96	0,306	0,157	Glutamate release inhibitor

97	0,326	0,192	Cytochrome P450 inhibitor
98	0,392	0,274	CYP3A2 substrate
99	0,306	0,204	Atherosclerosis treatment
100	0,365	0,265	Glyceryl-ether mono oxygenase inhibitor
101	0,352	0,255	Integrin antagonist
102	0,327	0,238	Dimethylaniline mono oxygenase (N-oxide-forming) inhibitor
103	0,314	0,229	Insulinotropin agonist
104	0,300	0,230	Protein-arginine deiminase inhibitor
105	0,321	0,281	Membrane permeability enhancer
106	0,308	0,273	(R)-Pantolactone dehydrogenase (flavin) inhibitor
107	0,375	0,349	Transplant rejection treatment
108	0,316	0,301	Antialcoholic
109	0,317	0,304	Convulsant
110	0,331	0,323	CYP3A1 substrate
111	0,349	0,363	Arrhythmogenic
112	0,335	0,350	Fibrinolytic
113	0,301	0,320	Membrane dipeptidase inhibitor
114	0,336	0,361	Adenylate cyclase stimulant

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References

1. Ghadimi S, Khajeh V. Synthesis, characterization, and prediction of biological activity of phosphoramide compounds. Journal of the Iranian Chemical Society 2007;4(3):325-331.
2. Maridass M, Raju G, Thangavel K, Ghanthikumar S. Prediction of Anti-HIV activity of flavoniod constituents through PASS. Ethnobotanical Leaflets 2008;12: 954-94.
3. Barnes CS, Loder JW. Structure of polygodial, a new sesquiterpene dialdehyde from Polygonum hydropiper L. Astralian J Chem 1962;15:322.

4. McCallion RF, Cole ALJ, Walker JRL, Blunt JW, Munro, MHG. Antibiotic substances from New Zealand plants.2. Polygodial, an anti-candida agent from *Pseudowintera colorata*. Planta Medica 1982;44:134-138.

5. Mendes GL, Santos ARS, Campos NM, Tratsk KS, Yunes RA, Fiho VC, Calixto JB. Anti-hyperalgesic properties of the extract and of the main sesquiterpene Polygodial isolated from the barks of *Drymis winteri* (Winteraceae). Life Sciences1998; 63:369-381.

6. Filimonov DA, Poroikov VV, Karaicheva EI, Kazaryan RK, Boudunova AP, Mikhailovsky EM, Rudnitskih AV, Goncharenko LV, Yu,V. *Computer-aided prediction of biological activity spectra of chemical substances on the basis of their structural formulae: computerized system PASS*. Experimental and Clinical Pharmacology (Rus) 1995; 8(2): 56-62.

7. Filimonov DA, Trapkov VA, Boudunova AP, Burova OA, Poroikov VV. Discovery of New Chemical Entry with Antiulcer Activity by Using Computer Aided Prediction. Abstr. XIVth International Symposium on Medicinal Chemistry, Maastricht, the Netherlands, 1996;1.12.

8. Fukuyama Y, Sato T, Miura I, Asakawa Y. Drimane-type sesqui-and nonsesquiterpene from *Polygonum hydropiper*. Phytochemistry1985; 24:1521-1524.

9. Alves TMA, Ribeira FL, Kloos H, Zani CL. Polygodial, the fungitoxic component from Brazilian medicinal plant *Polygonum punctatum*. Mem Inst Oswaldo Cruz,Rio de Janeiro 2001;96(6):831-833.