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In Silico Analysis of ADME-T Properties of Amentoflavone

Venkatesh[1,2], Shastri SL[1], Krishna V[1]* and Jayabaskaran C[2]

[1]Department of Post Graduate Studies and Research in Biotechnology, Kuvempu University, India

[2]Department of Biochemistry, Indian Institute of Science, India

Research Article

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***Corresponding author:** Krishna V, Department of Post Graduate Studies and Research in Biotechnology, Kuvempu University, Shankaraghatta 577451, Karnataka, India, Email: krishnabiotech2003@gmail.com

Abstract

Bioflavonoid, amentoflavone proven strong pharmacological properties. Prediction of *in silico* ADME-T properties by using PreADMET program. The result showed that amentoflavonehas good bioactivity, flexibility andpermeabilitywhich indicates that amentoflavone has potential to act as good drug.

Keywords: Amentoflavone; *Insilico*; ADME-T studies

Abbreviations: MW: Molecular Weight; TPSA: Topological Polar Surface Area; nON: Number Of Hydrogen Bond Acceptors; nOHNH: Number Of Hydrogen Bond Donors; WDI: World Drug Index; MDCK: Madin-Darby Canine Kidney; HIA: Human Intestinal Absorption; BBB: Blood Brain Barrier

Introduction

Bioflavonoid is one of unique classes of naturally-occurring flavonoids. The bioflavonoids particularly amentoflavone were previously reported in 127 plants [1] and has variety of bioactiveproperties such asantioxidant, anti-inflammatory, antisenescence, antitumor, antivirus, antimicrobial, central nervous system disorder, cardioprotective property, antimalarial activity, anti-ulcerogenic, analgesic, anti angiogenic, radioprotective and cytotoxic activity [2-10].

The World Drug Index (WDI) based on "rule-of-five" to identification of several critical properties of molecules that must to be considered as drug for oral administration [11]. The assessment of drug metabolism, pharmacokinetics, and toxicity in the early stage of drug development before proceedings to evaluate a compound in clinical studies. Number of tools available to predict absorption, distribution, metabolism, excretion, and toxicity (ADME-T) property.The various studies have been carried out to know the potential *in vitro* and *in vivo* property of Amentoflavone. Previously isolation methods of amentoflavone from *Semecarpusanacardium* have been reported (unpublished). But in the present study focused on *in silico* prediction of ADME-T properties of Amentoflavone.

Materials and Methods

Physicochemical and *Insilico* ADME-T studies

The MOL file and 'SMILES' of amentoflavone was procured from ChemSpider database (http://chemspider.com/). They are used as an input for *in silico* analysis. Physicochemical properties of compound were calculated using online Molinspiration cheminformatics server (http://www.molinspiration.com/). *Insilico* ADME-T property of Amentoflavone molecule was calculated by using a web-based application PreADME-T program (https://preadmet.bmdrc.kr/adme/ and https://preadmet.bmdrc.kr/toxicity/) [12].

Results and Discussion

The present study demonstrates the physiochemical and ADME-T properties of amentoflavone.

IUPAC Name : 8-[5-(5,7-dihydroxy-4-oxochromen-2-yl)-2-hydroxyphenyl]-5,7-dihydroxy-2-(4-hydroxyphenyl) chromen-4-one
SMILES:C1=CC(=CC=C1C2=CC(=O)C3=C(O2)C(=C(C=C3O)O)C4=C(C=CC(=C4)C5=CC(=O)C6=C(C=C(C=C6O5)O)O)O)O

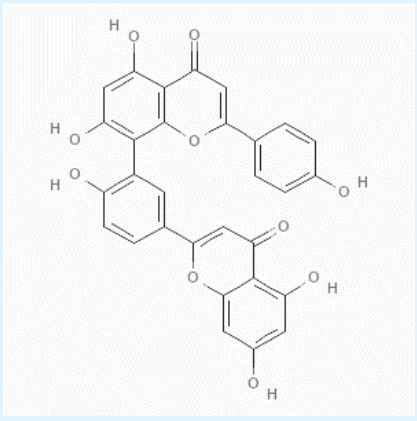

Figure 1: Amentoflavone.

Physicochemical Properties

The physicochemical properties such as lipophilicity (clogP), polar surface area, molecular weight (MW) and aqueous solubility (logS), these properties affect absorption and bioavailability of drug molecule. According to the predicted data, two violations of Lipinskis Rule (Rule of Five) were identified (MW>500 and NHorOH>5). The TPSA (Topological Polar Surface Area) is another important physicochemical property used to predict drug distribution attributes based on sum of all polar atoms such as oxygen, nitrogen and attached hydrogen value and number of rotatable bonds indicate good bioavailability [13]. The TPSA value is 181.79 Å and number of rotatable bonds found to be 3. Rotatable polar atomic bonds increase the flexibility of molecules for more adaptable and efficient interaction with the enzyme active site and the value of TPSA of amentoflavone indicates good oral bioavailability (Table 1).

Sl. No.	Compound (Chemspider ID)	Physicochemical properties						
1	Amentoflavone (4444919)	MW	miLogP	TPSA (Å)	nON	nOHNH	nrotb	Volume
		538.46	5.16	181.79	10	6	3	435.46

Table 1: Physicochemical properties of Amentoflavone
MW- Molecular Weight, miLogP -Octanol-water partition coefficient logP developed at molinspiration, TPSA - Topological Polar Surface Area, nON - number of hydrogen bond acceptors, nOHNH- number of hydrogen bond donors, Volume - molecule volume.

In silico ADME-T studies

The HIA (human intestinal absorption) value is 100%. This indicates that amentoflavone can be well absorbed via intestinal tract. In addition, amentoflavone shows good permeability to Caco2 cell (22.2815) (heterogeneous human epithelial colorectal adenocarcinoma cells) and to MDCK cell (Madin-Darby Canine Kidney) model 204.401. In distribution phase, the PPB (Plasma Protein Barrier) binding assessment of amentoflavone exhibit strong binding energy with plasma proteins (predicted value -1). Generally weak plasma protein binding compounds exist freely for transport across the cell membrane and also for interaction with target. In addition, BBB (Blood Brain Barrier) penetration revealed that the compound showed low absorption in CNS (predicted value 1.49973) and showed least skin permeability (-1.86648). In toxicity phase, the carcinogenic and mutagenic effects of compound were evaluated. Ames test is a simple method to test mutagenicity, amentoflavone had shown positive result indicating that the compound act as mutagen. It also showed negative carcinogenicity for mice and positive carcinogenicity for rats (Table 2).

ADME							Toxicity		
Chemspider ID	HIA (%)	PPB (%)	BBB (%)	Cacok2 (nm/sec)	Skin Permeability	MDCK (nm/sec)	Mutagenicity	Rodent Carcinogenicity	
								Carcino Mouse	Carcino Rat
4444919	100	-1.#IND00	1.49973	22.2815	-1.8665	204.401	Mutagen	Negative	Positive

Table 2: ADME-Toxic properties of Amentoflavone

Conclusion

The amentoflavone have been shown to have a wide range of biological and pharmacological activities. Present study also predicted that amentoflavone is a potential bioactive compound and this predicted data may help for further research analysis of drug development.

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References

1. Yu S, Yan H, Zhang L, Shan M, Chen P, et al. (2017) A Review on the Phytochemistry, Pharmacology, and Pharmacokinetics of Amentoflavone, a Naturally-Occurring Biflavonoid. Molecules 22(2): 299.

2. Okigawa M, Hwa CW, Kawano N, Rahman W (1971) Biflavones in Selaginella species. Phytochemistry 10: 3286-3287.

3. Saroni Arwa P, Zeraik ML, Ximenes VF, da Fonseca LM, Bolzani Vda S, et al. (2015) Redox-active biflavonoids from *Garciniabrasiliensis* as inhibitors of neutrophil oxidative burst and human erythrocyte membrane damage. Journal of Ethnopharmacology 174: 410-418.

4. Abdallah HM, Almowallad FM, Esmat A, Shehata IA, Abdel-Sattar EA (2015) Anti-inflammatory activity of flavonoids from Chrozophoratinctoria. Phytochemistry Letter 13: 74-80.

5. Park NH, Lee CW, Bae JH, Na YJ (2011) Protective effects of amentoflavone on Lamin A-dependent UVB-induced nuclear aberration in normal human fibroblasts. Bioorganic & Medicinal Chemistry Letters 21: 6482-6484.

6. Ndongo JT, Issa ME, Messi AN, Mbing JN, Cuendet M, et al. (2015) Cytotoxic flavonoids and other constituents from the stem bark of Ochnaschweinfurthiana. Natural Product Research 29(17): 1684-1687.

7. Coulerie P, Nour M, Maciuk A, Eydoux C, Guillemot JC, et al. (2013) Structure-activity relationship study of biflavonoids on the Dengue virus polymerase DENV-NS5 RdRp. Planta Medica 79(14): 1313-1318.

8. Hwang IS, Lee J, Jin HG, Woo ER, Lee DG (2012) Amentoflavone stimulates mitochondrial dysfunction and induces apoptotic cell death in Candida albicans. Mycopathologia 173(4): 207-218.

9. Zhang Z, Sun T, Niu JG, He ZQ, Liu Y, et al. (2015) Amentoflavone protects hippocampal neurons: Anti-inflammatory, antioxidative, and antiapoptotic effects. Neural Regeneration Research 10(7): 1125-1133.

10. Zheng XK, Liu CX, Zhai YY, Li LL, Wang XL, et al. (2013) Protection effect of amentoflavone in Selaginella tamariscina against TNF-alpha-induced vascular injury of endothelial cells Acta Pharmacologica Sinica 48(9): 1503-1509.

11. Lipinski CA, Lombardo F, Dominy BW, Feeney PJ (1997) Experimental and computational approaches to estimate solubility and permeability in drug discovery and development settings. Advanced Drug Delivery Reviews 23: 3-25

12. Kandagalla S, Sharath BS, Bharath BR, Manjunatha H (2017) Molecular docking analysis of curcumin analogues against kinase domain of ALK5. In Silico Pharmacology 5: 15.

13. Clark DE (1999) Rapid Calculation of Polar Molecular Surface Area and Its Application to the Prediction of Transport Phenomena. 2. Prediction of Blood–brain Barrier Penetration. Journal of Pharmaceutical Sciences 88(8): 815-821.