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# Characterization of isolated bioactive phytoconstituents from *Flacourtia indica* as potential phytopharmaceuticals - An *in silico* perspective

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**Abstract**
The dependence of mankind for therapeutic applications on plants dates back to the start of the human race. Natural remedies from ethnobotanicals are found to be safe and cost effective. Due to the poor pharmacokinetic profiles and toxicity problems many synthetic drugs often fails to enter the market thus, the pharmacologically active compounds from plants continued to provide an important source of novel drug leads. The early inclusion of pharmacokinetics consideration in the drug discovery process using *in silico* methods is becoming popular due to improved generation of software's. The problems with conventional method required time-consuming multi-step processes against a battery of *in vivo* biological screening and high cost thus, *In silico* prediction of the pharmacokinetic parameters, biological properties and toxicity due to advent of chemo-informatics tools, has reduced the cost dramatically and early application in drug design are realized. The present investigation deals with computational evaluation of six isolated phytocompounds from *Flacourtia indica* for their pharmacological potential and biological activities. These compounds were evaluated for drug likeness properties, bioactivity score, ADME/T profiles, and health affects by using various bioinformatics tools. The result indicated that all the six compounds analyzed were non mutagens, non-carcinogens and having good drug-likeness properties were seen. The ADMET parameters and probability of health effects were analyzed by admet SAR and ACD/I-Lab online tools respectively and results shows the ADMET and probability of health effects values are also in satisfying ranges. Pharmacological activities of these compounds were predicted individually using PASS server many different pharmacological activities and mechanisms of action shown by these compounds were reported. The results of our analysis clearly depict that all six phytocompounds were having good pharmacokinetic profiles with numerous biological activities. These compounds can be further studied *in vitro* and *in vivo* for the discovery of novel preventive and therapeutic drug.

**Keywords:** *Flacourtia indica,* phytopharmaceuticals, ADMET, PASS, *in silico,* pharmacokinetics, drug discovery

## Introduction
Plants have been exploited over the millennia for human welfare in the promotion of health and as therapeutic drugs. Most of the developing countries such as China, India, Sri Lanka and a few others endowed with vast resources of medicinal and aromatic plants. Plants being rich sources of secondary metabolites such as alkaloids, terpenoids, triterpenies, flavanoids, tannins, and phenolic compounds etc. which are responsible for various biological activities have been used as treatment for various ailments (de-Fathima *et al*., 2006) [7]. In the later mediaeval period, Islamic part of the world has flourished the herbalism (David taylor, 2014) and Arab's were encouraged to use plants and fruits as nutraceuticals, the holy Quran mentions many plants as nutraceuticals so that the mankind can enjoy and benefit from their nutritional and health values. Among some of the ethnobotanicals mentioned in the holy Quran and Hadith by the Holy Prophet Mohammed ﷺ (Peace Be Upon Him) are Sweet flag, Myrrh, Memcylon (Tintura), Barley, Sweet basil, Pomegranate, grapes, citrus, melon, squash, Figs, date palm, honey, olive oil, and black seeds etc,.*(*Rahman *et al., 2008;* Ahmad *et al.,* 2009) [19, 1]. The statement of Holy Prophet Mohammed ﷺ (Peace Be upon Him) that "there is no disease that Allah has created, except that He also has created its treatment" encouraged Mankind to engage in medical research and seek out a cure for every disease known to them (Ahmed and Hasan, 2015). Medicinal plants, the backbone of traditional medicine with excessive pharmacological studies are the potential source of lead compounds in drug development (Mathew *et al.,* 2016) [15]. Modern pharmacopoeia still contains at least 25% drugs derived from plants (De Silva, 1997) [8]. Since many synthetic drugs often fail to enter

the market as a result of poor pharmacokinetic and pharmacodynamics profiles (Ntie-Kang, 2013) [17], therefore phytopharmaceuticals are preferred since Plants have been evolved through biological validation and therefore induce less toxicity and side effects as compared to synthetic drugs (Mathew *et al., 2016*) [15]. The use of plants in the control and treatment of diseases in recent years has gained considerable importance and major sources of biologically active and high pharmacological active compounds are from plants and fruits (WHO Report, 2002) [22].

The objective of drug design is to find a chemical compound that can fit to a specific cavity called binding pocket cleft on a protein target both geometrically and chemically. After passing the animal tests and human clinical trials, this compound becomes a drug available in market to patients. The conventional drug design methods include random screening of chemicals found in nature or synthesized in laboratories. The problems with conventional method required time-consuming multi-step processes against a battery of *in vivo* biological screening and high cost. Modern approach including structure-based drug design with the help of informatics technologies and computational methods has speeded up the drug discovery process in an efficient manner. Remarkable progress has been made during the past five years in almost all the areas concerned with drug design and discovery. An improved generation of software's with easy operation and superior computational tools to generate chemically stable and worthy compounds with refinement capability has been developed. These tools can tap into cheminformation to shorten the cycle of drug discovery, and thus make drug discovery in more efficiency, cost effectiveness, time saving, and will provide strategies for combination therapy in addition to overcoming toxic side effect (Mandal *et al.*, 2009; Baldi, 2010; Sharma and Sarkar, 2013) [14, 5, 21].

The present investigation aimed to assess the pharmacokinetics, pharmacological properties and biological activities of the isolated phytocompounds from *Flacourtia indica* (BURM.F.) Merr. By computational approach. *Flacourtia indica* (Burm.f.) Merr, belonging to the family Flacourtiaceae, is a small deciduous thorny shrub indigenous to the Indian Peninsula. *Flacourtia indica* is very popular and used as folklore medicine to treat various diseases, fruits are used in the treatment of jaundice and enlarged spleen, seeds are used as rheumatic pain, bark is applied to the body duting intermittent fever and root is used in the nephritic colic (Eramma and Gayathri, *2013;* Sashidhara *et al.,* 2013) [9, 20] isolated and purified six phytocompounds viz.,"(1) 2-(2-benzoyl-b-D-glucopyranosyloxy)-7-(1a,2a,6a-trihydroxy-3-oxocyclohex-4-enoyl)-5-hydroxy benzyl alcohol, (2) poliothrysoside, (3) catechin-[5,6-e]-4b-(3,4-dihydroxy phenyl)dihydro-2(3H)-pyranone, (4) 2-(6-benzoyl-b-D-glucopyranosyloxy)-7-(1a,2a,6a-trihydroxy-3-oxocyclo hex-4-enoyl)-5-hydroxybenzyl alcohol (5), chrysoeriol-7-O-b-D-glucopyranoside and (6) mururin A" by applying series of chromatographic techniques and Experimentally reported that Compound 6 significantly inhibited the in vitro growth of both a chloroquine-sensitive(3D7) and a chloroquine-resistant (K1) strain of Plasmodium falciparum (Sashidhara *et al.*, 2013) [20].

## Methods and Implications

### Preparation of phyto-ligands

The six phytocompounds isolated from *Flacourtia indica* (Sashidhara *et al.,* 2013) [20] *viz*., "(1) 2-(2-benzoyl-b-D-glucopyranosyloxy)-7-(1a,2a,6a-trihydroxy-3-oxocyclohex-4-enoyl)-5-hydrox -ybenzylalcohol, (2) poliothrysoside, (3) catechin-[5,6-e]-4b-(3,4- dihydro xyphenyl) dihydro-2(3H)-pyranone, (4) 2-(6-benzoyl-b-D-glucopyranosyloxy)-7-(1a,2a,6a-trihydroxy-3-oxocyclo hex-4-enoyl)-5-hydroxybenzyl alcohol (5), chrysoeriol-7-O-b-D-glucopyranoside and (6) mururin A" were tested for their pharmacological Potential and biological activity for use as promising therapeutic compounds. The 2D and 3D structures of these isolated phytocompounds were obtained from online server's *viz*., PubChem (http://pubchem.ncbi.nlm.nih.gov/) and ChemSpider (http://www.chemspider.com/) and each chemical compound was constructed using ACD/ Chemsketch bioinformatics tool and saved in the '.mol' format.

### *In silico* pharmacokinetics analysis

#### (a) Prediction Drug-likeness properties

Drug-likeness of a chemical compound is equilibrium amongst the molecular properties of a compound which directly affects biological activity, pharmacodynamics and pharmacokinetics of a drug in human body (Menezes *et al.*, 2011) [16]. The "drug-likeness" test was carried out using Lipinski's "Rule of Five", ro5 (Lipinski *et al*., 1997). The distributions of the compound molecular weights (MW), calculated lipophilicity (logp), number of hydrogen bond acceptors (HBA) and number of hydrogen bond donors (HBD) were used to assess the "drug-likeness" of Compounds (Ntie-Kang F, 2013) [17]. Depending on these four molecular descriptors, the approach generates a vigilant about apparent absorption trouble; the rule states that most "druglike" molecules must have log P≤ 5, molecular weight ≤ 500, number of hydrogen bond acceptors ≤ 10, and number of hydrogen bond donors ≤ 5. Molecules violating more than one of these rules may have problems with oral bioavailability (Paramashivam *et al.,* 2015) [18].

#### (b) Prediction of bioactivity scores of Phytocompounds Molinspiration

Molinspiration tool was used In order to predict bioactivity score, Molinspiration is a free on-line cheminformatics services for calculation of important molecular properties as well as prediction of bioactivity score for the most important phytoconstituents drug targets such as GPCR ligand, Ion channel modulator, Kinase inhibitor, Nuclear receptor ligand, Protease inhibitor, Protease inhibitor and Enzyme inhibitor (Balasundaram *et al.,* 2016 ) [4].

#### (c) ADME/Tox Predictions by AdmetSAR

Pharmacokinetics (PK) plays a key role throughout pharmaceutical research and development (Alavijeh *et al.,* 2005) [3]. ADMET is an abbreviation in pharmacokinetics for "absorption, distribution, metabolism, excretion and Toxicity." A set of algorithms are involved in predicting the pharmacological activity of a molecule as a prospective drug *(*Lydia and Sudarsanam, 2015) [13]. The pharmacokinetic properties such as Absorption, Distribution, Metabolism, Excretion and the Toxicity of the compounds can be predicted using admet SAR (http:// www.admetexp.org) online database. It provides the latest and most comprehensive manually curated data for diverse chemicals associated with known ADMET profiles.

**(d) Computation Lethal Dose $_{50}$ and probability of health effects using ACD/I-Lab**

ACD/I labs is a free online server which consist of a set of molecular and ADMET descriptors. The probability of health effects and physicochemical properties was predicted using lethal dose$_{50}$ ($LD_{50}$) value. The comparative analysis of ligand molecules $LD_{50}$ values were studied in mouse and rat by intra peritoneal, oral, intravenous, subcutaneous and the probability of toxic health effects were checked in blood, cardiovascular system, gastro intestinal system, kidney, liver, and lung tissues.

**(e) Predictions Biological activity by PASS Server**

PASS (Predicted Activity Spectrum for Substances) server (http://195.178.207.233/PASS/), this server predicted activity spectrum of a chemical compound as Pa (probable activity) and Pi (probable inactivity). The set of pharmacological effects, mechanisms of action, and specific toxicities, that might be exhibited by a particular compound in its interaction with biological entities, and which is predicted by PASS (Paramashivam *et al.,* 2015) [18], Prediction of this spectrum by PASS was based on structural activity relationship (SAR) analysis of the training set containing 205,000 plus compounds having more than 3750 kinds of Pharmacological effects and biological activities (Goel *et al.,* 2011) [10]. The compounds showing higher Pa value than Pi are the only constituents considered as possible for a particular pharmacological activity (Khurana *et al.,* 2011; Goel *et al.,* 2011) [11, 10].

**Results and Discussion**

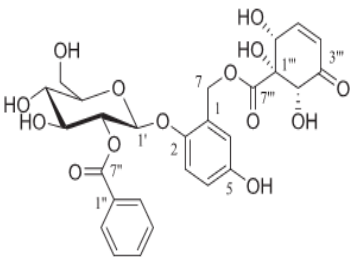
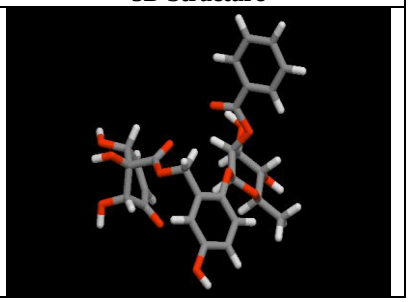
Plants belonging to family Flacourtiaceae are well known for their biological and ethnomedicinal properties and are used as folklore medicine in the treatment of various ailments in India. The structures of the six isolated compounds were retrieved from pubchem and chemspider servers which are represented in table 1. pharmacokinetic and QSAR properties of the compounds were checked for their drug likeness, drug score, bioactivity score, ADME/T profile, and health affect by using various software's mentioned in Section 2. The drug likeliness and drug score of the compounds were predicted by Lipinski's "rule of five" and the results are depicted in Table. 2 and graphical representation of drug likeness score was shown in the figure (fig.1-fig.6).Out of six phytocompounds, after computation it was found that compound 2 and 6 are significantly follows the Ro5 and other compounds violates one or two parameters viz. acceptable. The drug likeness score of all the compounds are in acceptable ranges but compound 3, 5 and 6 has the highest score when compare to others.

The bioactivity score of the compounds for the drug targets such as GPCR ligand, Ion channel modulator, Kinase inhibitor, Nuclear receptor ligand, Protease inhibitor, Protease inhibitor and Enzyme inhibitor are evaluated using molinspiration tool are listed in the table 3. From the data obtained, one can notice that all the six compounds possess bioactive score in acceptable ranges. The ADMET analysis in early stages of drug discovery is a very crucial since most of the compounds fails due to poor pharmacokinetics properties and toxicity problems. ADMET properties such as blood brain barrier, Caco-2 cell permeability, Human intestinal absorption, P-gp substrate, P-gp inhibitor, Ames mutagenicity and carcinogenicity were analyzed through computational methods and reported in table 4. The result shows that all the six compounds are passes the ADMET filters with no carcinogenicity and no mutagenicity and all the parameters are in acceptable ranges which are the signs of good pharmacokinetics profiles.

The lethal dose 50 ($LD_{50}$) values of the six compounds were analyzed for the acute toxicity that has administered through oral, intraperitoneal, intravenous and subcutaneous on mouse / rat models and also toxicity with reference to different organs to check adverse effects on organs and their systems are tested and the results are mentioned in table 5. The overall results suggested that all the six phytoconstituents had less toxic effect on internal tissues and no side-effect were observed in the tested dosages.

The pharmacological effects and biological activities of six compounds were analyzed through PASS online server; the values of Pa and Pi vary between 0.000 and 1.000. Only activities with Pa > Pi are considered as possible for a particular compound. If Pa > 0.7, the probability of experimental pharmacological action is high and if 0.5 < Pa < 0.7, probability of experimental pharmacological action is less. The tested compounds shows many pharmacological activities and mechanism of actions which were represented in table 6.

**Table 1:** Isolated compounds from *Flacourtia indica* with their 2D and 3D structures.

| Sl no | Compound | 2D Structure | 3D Structure |
|---|---|---|---|
| 1 | 2-(2-benzoyl- b-D-glucopyranosyloxy)-7-(1 a,2 a,6a trihydroxy-3-oxocyclohex-4-enoyl)-5-hydroxy benzyl alcohol |  |  |

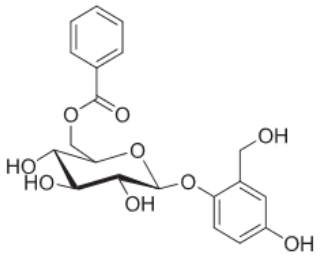
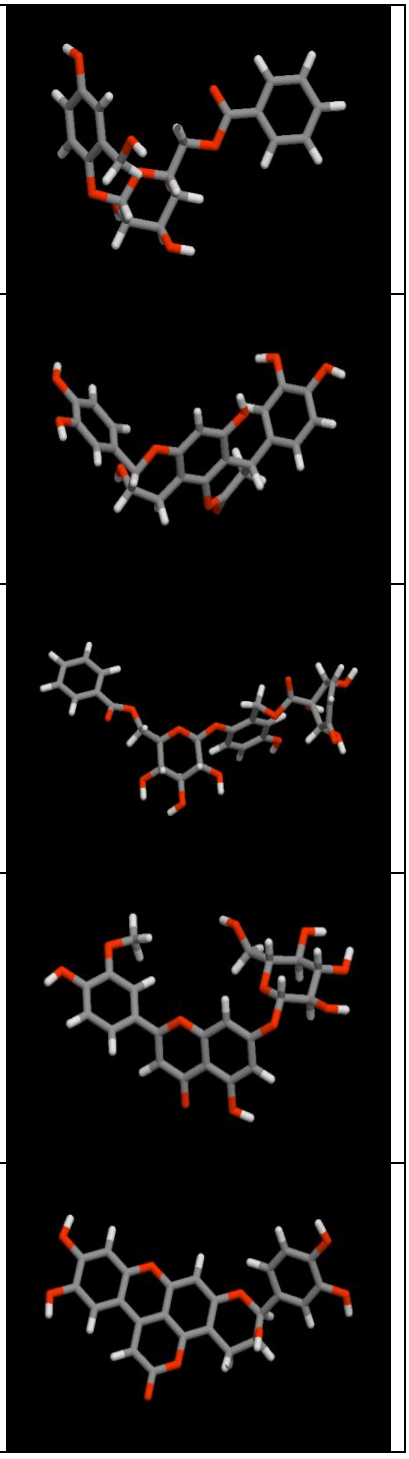
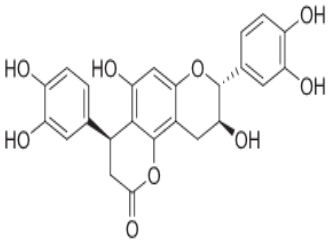
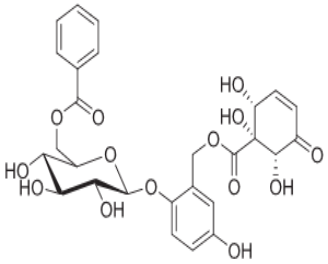
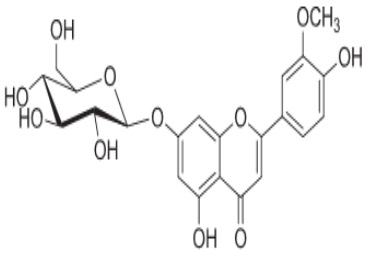
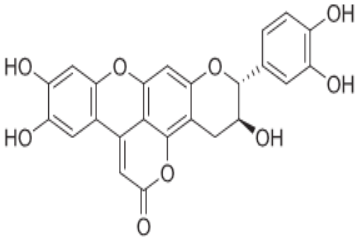
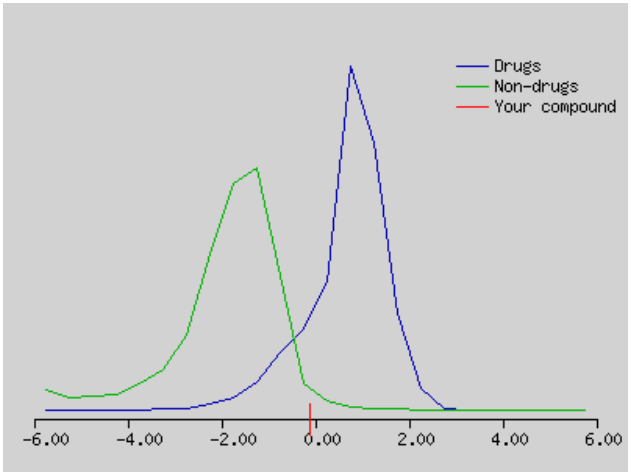
| | | | |
|---|---|---|---|
| 2 | poliothrysoside |  |  |
| 3 | catechin-[5,6-e]-4b-(3,4dihydroxyphenyl)dihydro-2(3H)-pyranone |  | |
| 4 | 2-(6-benzoyl-b-D glucopyranosyloxy)-7-(1a,2 a,6 a-trihydroxy-3-oxocyclohex-4-enoyl)-5-hydroxybenzyl alcohol |  | |
| 5 | chrysoeriol-7-O- b-D-glucopyranoside |  | |
| 6 | mururin A |  | |

**Table 2:** Lipinski rule of five and Drug-likeness properties prediction using Molsoft online program

| Compound | Molecular Formula | Molecula Weight | Hydrogen Bond accepter (HBA) | Hydrogen Bond Donator ( HBD) | Mol LogP | Number of rotatable bonds | Drug-likeness model score |
|---|---|---|---|---|---|---|---|
| 1 | C27 H28 O14 | 576.15 | 14 | 7 | -2.21 | 10 | -0.10 |
| 2 | C20 H22 O9 | 406.13 | 9 | 5 | 0.14 | 7 | -0.10 |
| 3 | C24 H20 O9 | 452.11 | 9 | 6 | 2.64 | 2 | 1.18 |
| 4 | C27 H28 O14 | 576.15 | 14 | 7 | -2.07 | 10 | -0.19 |
| 5 | C22 H22 O11 | 462.12 | 11 | 6 | 0.28 | 5 | 0.77 |
| 6 | C24 H16 O9 | 448.08 | 9 | 5 | 3.76 | 1 | 0.62 |



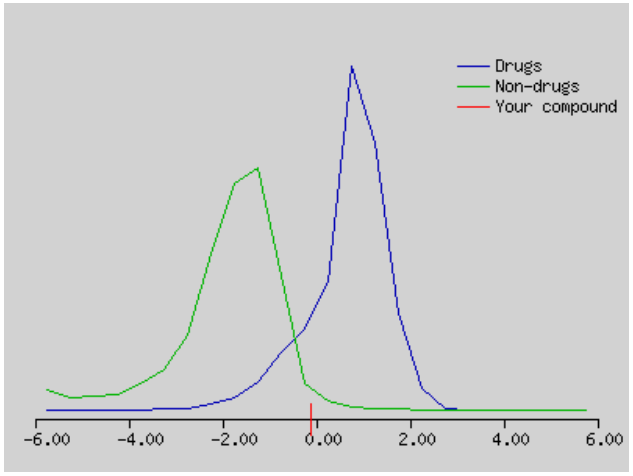
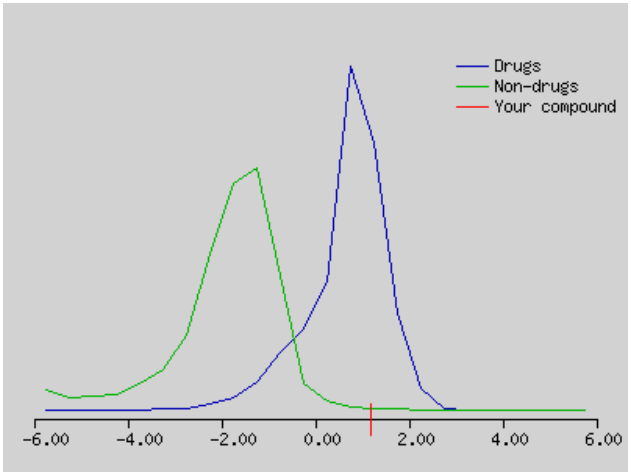




**Fig 1:** Drug-likeness model score: -0.10 **Fig 2:** Drug-likeness model score: -0.10



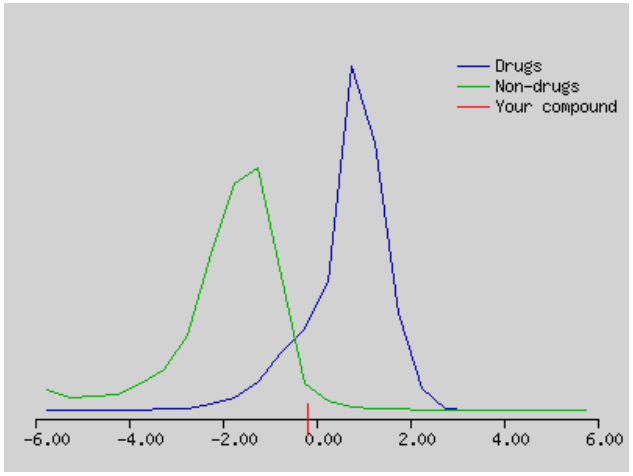
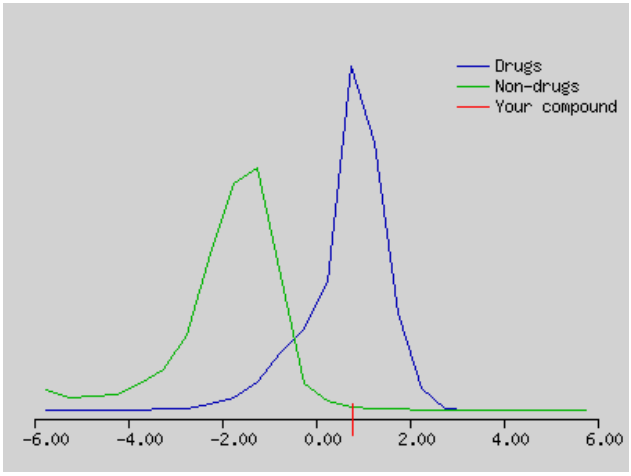




**Fig 3:** Drug-likeness model score: 1.18 **Fig 4:** Drug-likeness model score: -0.19



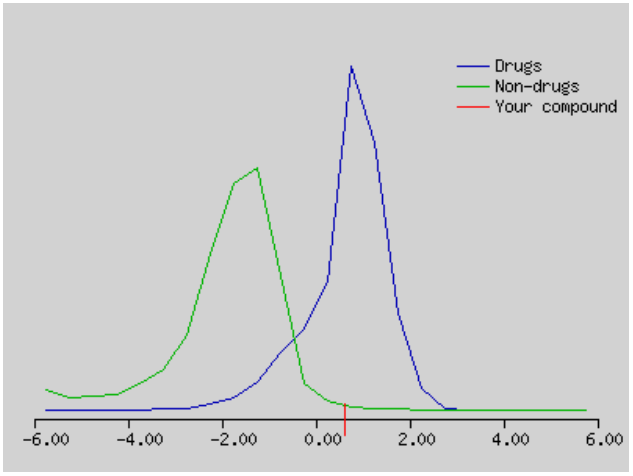




**Fig 5:** Drug-likeness model score: 0.77 **Fig 6:** Drug-likeness model score: 0.62

**Table 3:** Bioactivity scores of Phytocompounds predicted by Molinspiration.

| Compond | GPCR ligand | Ion channel modulator | Kinase inhibitor | Nuclear receptor ligand | Protease inhibitor | Enzyme inhibitor |
|---|---|---|---|---|---|---|
| 1 | 0.09 | -0.29 | -0.28 | 0.11 | 0.14 | 0.26 |
| 2 | 0.03 | 0.01 | -0.12 | 0.12 | 0.01 | 0.26 |
| 3 | 0.25 | 0.03 | -0.17 | 0.33 | 0.21 | 0.32 |
| 4 | 0.06 | -0.26 | -0.27 | 0.13 | 0.12 | 0.24 |
| 5 | 0.05 | -0.07 | 0.14 | 0.21 | -0.06 | 0.37 |
| 6 | 0.04 | -0.32 | -0.08 | 0.42 | -0.15 | 0.27 |

**Table 4:** ADME/TOX and pharmacological parameter assessment of phytocompounds predicted using admetSAR toolbox

| Compond | PlogBB[a] | PCaco[b] | log$_{HIA}$[c] | logpGI (substrate)[d] | logpGI (non-inhibitor)[e] | PlogS[f] | AMES Toxicity | Carcin-ogens |
|---|---|---|---|---|---|---|---|---|
| 1 | 0.6121 | 0.8530 | 0.7902 | 0.7055 | 0.7135 | -1.3448 | NT | NC |
| 2 | 0.5000 | 0.8892 | 0.7559 | 0.5911 | 0.8115 | -0.9489 | NT | NC |
| 3 | 0.6208 | 0.8591 | 0.9015 | 0.6008 | 0.9421 | -3.5109 | NT | NC |
| 4 | 0.5993 | 0.8427 | 0.8541 | 0.7230 | 0.7362 | -1.5114 | NT | NC |
| 5 | 0.9247 | 0.8957 | 0.7769 | 0.6724 | 0.8575 | -2.3177 | NT | NC |
| 6 | 0.6553 | 0.8641 | 0.9450 | 0.5638 | 0.9077 | -3.4816 | NT | NC |

[a]-Predicted blood/brain barrier partition coefficient (concern value is −3.0 to 1.0), [b]-predicted Caco-2 cell permeability in nm/s (acceptable range: −1 is poor, 1 is great), [c]-predicted human intestinal absorption in nm/s (acceptable range: 0 poor, >1 great), [d]-predicted P-gp substrate in nm/s (acceptable range of −5 is poor, 1 is great), [e]-predicted P-glycoprotein inhibitor in nm/s (accepted range: 0-1), [f]-predicted aqueous solubility, (concern value is −6.5 to –0.5). P-gp: P-glycoprotein, HIA: Human intestinal absorption, ADME: Absorption, distribution, metabolism, excretion NT: Non Ames toxic, NC: non carcinogens.

**Table 5:** LD 50 and probability of health effects of Phytocompounds predicted using ACD/I-Lab 2.0

| ADME-TOX Parameters | 1 | 2 | 3 | 4 | 5 | 6 |
|---|---|---|---|---|---|---|
| $LD_{50}$ mouse[1] (mg/kg, intraperitoneal) | 1100 | 1000 | 490 | 900 | 1100 | 470 |
| $LD_{50}$ mouse[1] (mg/kg, oral) | 4900 | 1800 | 3000 | 5900 | 360 | 2100 |
| $LD_{50}$ mouse[1] (mg/kg, intravenous) | 800 | 500 | 69 | 600 | 67 | 110 |
| $LD_{50}$ mouse[1] (mg/kg, subcutaneous) | 2500 | 1500 | 140 | 4200 | 190 | 28 |
| $LD_{50}$ Rat[1] (mg/kg, intraperitoneal) | 560 | 570 | 1900 | 440 | 930 | 2400 |
| $LD_{50}$ Rat[1] (mg/kg, oral) | 11000 | 2900 | 3100 | 10000 | 930 | 3100 |
| Probability of blood effect[2] | 0.98 | 0.63 | 1 | 0.95 | 1 | 0.98 |
| Probability of cardiovascular system effect[2] | 0.97 | 0.86 | 0.97 | 0.96 | 0.92 | 0.99 |
| Probability of gastrointestinal system effect[2] | 0.96 | 0.07 | 0.99 | 0.97 | 0.94 | 1 |
| Probability of kidney effect[2] | 0.62 | 0.24 | 0.86 | 0.63 | 0.63 | 0.9 |
| Probability of liver effect[2] | 0.71 | 0.19 | 0.84 | 0.72 | 0.8 | 0.97 |
| Probability of lung effect[2] | 0.46 | 0.42 | 0.98 | 0.46 | 0.52 | 0.97 |

[1]Estimates LD 50 value in mg/kg after intraperitoneal, oral, intravenous and subcutaneous administration to mice and rat, [2]Estimates probability of blood, gastrointestinalsystem, kidney, liver and lung effect at therapeutic dose range, 1-6 represents the phytocompounds and the drugs with moderate effect on reliability index (>0.5), the drugs with border line effect on reliability index (>0.3, <0.5), LD50: Lethal dose50.

**Table 6:** Predicted Pa and Pi values of phytocompounds using PASS online server.

| Compounds | Pa[*] | Pi[#] | Predicted Pharmacological activity | pa | pi | Predicted Pharmacological Activity |
|---|---|---|---|---|---|---|
| **2-(2-benzoyl- b-D-glucopyranosyloxy)-7-(1 a,2 a,6 a-trihydroxy-3-oxocyclohex-4-enoyl)-5-hydroxybenzyl alcohol** | 0,928 | 0,006 | CDP-glycerol glycerophosphotransferase inhibitor | 0,799 | 0,005 | Anticarcinogenic |
| | 0,906 | 0,010 | Membrane integrity agonist | 0,747 | 0,003 | Monophenol monooxygenase inhibitor |
| | 0,898 | 0,006 | CYP2H substrate | 0,752 | 0,010 | UDP-N-acetylglucosamine 4-epimerase inhibitor |
| | 0,862 | 0,006 | Anaphylatoxin receptor antagonist | 0,749 | 0,008 | Mucinaminylserine mucinaminidase inhibitor |
| | 0,850 | 0,007 | Antineoplastic | 0,751 | 0,018 | Beta-adrenergic receptor kinase inhibitor |
| | 0,850 | 0,009 | Sugar-phosphatase inhibitor | 0,751 | 0,018 | G-protein-coupled receptor kinase inhibitor |
| | 0,840 | 0,004 | 3-Phytase inhibitor | 0,734 | 0,008 | Antiprotozoal (Leishmania) |
| | 0,847 | 0,011 | Benzoate-CoA ligase inhibitor | 0,728 | 0,014 | Exoribonuclease II inhibitor |
| | 0,841 | 0,012 | Alkenylglycerophosphocholine hydrolase inhibitor | 0,737 | 0,025 | Membrane permeability inhibitor |
| | 0,830 | 0,003 | Lactase inhibitor | 0,710 | 0,005 | Fructan beta-fructosidase inhibitor |
| | 0,818 | 0,005 | Antiinfective | | | |
| **poliothrysoside** | 0,973 | 0,001 | Monophenol monooxygenase inhibitor | 0,825 | 0,001 | Glucan 1,6-alpha-glucosidase inhibitor |
| | 0,966 | 0,002 | Membrane integrity agonist | 0,822 | 0,001 | 4-Alpha-glucanotransferase inhibitor |
| | 0,951 | 0,003 | Alkenylglycerophosphocholine hydrolase inhibitor | 0,827 | 0,006 | NAD(P)+-arginine ADP-ribosyltransferase inhibitor |
| | 0,949 | 0,002 | Sugar-phosphatase inhibitor | 0,822 | 0,003 | Cyclomaltodextrinase inhibitor |
| | 0,946 | 0,004 | CDP-glycerol glycerophosphotransferase inhibitor | 0,824 | 0,006 | Glucan endo-1,6-beta-glucosidase inhibitor |
| | 0,932 | 0,002 | 3-Phytase inhibitor | 0,814 | 0,001 | 4-Coumarate-CoA ligase inhibitor |
| | 0,933 | 0,003 | Antiinfective | 0,814 | 0,002 | Laminaribiose phosphorylase inhibitor |
| | 0,926 | 0,003 | Membrane permeability inhibitor | 0,813 | 0,005 | UDP-glucuronosyltransferase substrate |
| | 0,915 | 0,002 | Beta-mannosidase inhibitor | 0,808 | 0,003 | Phenylacetate-CoA ligase inhibitor |
| | 0,915 | 0,002 | Mucinaminylserine mucinaminidase inhibitor | 0,772 | 0,009 | Membrane integrity antagonist |
| | 0,916 | 0,003 | Anaphylatoxin receptor antagonist | 0,771 | 0,010 | Immunostimulant |
| | 0,909 | 0,002 | Fructan beta-fructosidase inhibitor | 0,765 | 0,004 | Phosphoinositide 5-phosphatase inhibitor |
| | 0,905 | 0,003 | Exoribonuclease II inhibitor | 0,764 | 0,005 | Hepatoprotectant |
| | 0,905 | 0,005 | Benzoate-CoA ligase inhibitor | 0,766 | 0,007 | Lipid metabolism regulator |

| | | | | | | |
|---|---|---|---|---|---|---|
| | 0,896 | 0,003 | Cholesterol antagonist | 0,761 | 0,004 | Phosphatidylglycerophosphatase inhibitor |
| | 0,894 | 0,003 | UDP-N-acetylglucosamine 4-epimerase inhibitor | 0,761 | 0,007 | Vasoprotector |
| | 0,888 | 0,003 | Antihypercholesterolemic | 0,761 | 0,008 | Nucleotide metabolism regulator |
| | 0,885 | 0,002 | Lactase inhibitor | 0,753 | 0,003 | H+-exporting ATPase inhibitor |
| | 0,879 | 0,003 | Glucan endo-1,3-beta-D-glucosidase inhibitor | 0,751 | 0,003 | Free radical scavenger |
| | 0,876 | 0,003 | Levanase inhibitor | 0,749 | 0,004 | N-acylmannosamine kinase inhibitor |
| | 0,877 | 0,006 | Beta-adrenergic receptor kinase inhibitor | 0,747 | 0,005 | Antithrombotic |
| | 0,877 | 0,006 | G-protein-coupled receptor kinase inhibitor | 0,739 | 0,004 | Mycothiol-S-conjugate amidase inhibitor |
| | 0,864 | 0,001 | Laxative | 0,736 | 0,003 | Lactose synthase inhibitor |
| | 0,854 | 0,003 | Anthranilate-CoA ligase inhibitor | 0,738 | 0,006 | IgA-specific metalloendopeptidase inhibitor |
| | 0,856 | 0,005 | Fucosterol-epoxide lyase inhibitor | 0,731 | 0,001 | Oligo-1,6-glucosidase inhibitor |
| | 0,850 | 0,002 | Alkenylglycerophosphoethanolamine hydrolase inhibitor | 0,734 | 0,009 | Glyceryl-ether monooxygenase inhibitor |
| | 0,838 | 0,002 | Beta-amylase inhibitor | 0,731 | 0,008 | Antiprotozoal (Leishmania) |
| | 0,838 | 0,004 | Ribulose-phosphate 3-epimerase inhibitor | 0,723 | 0,002 | Glucan 1,4-beta-glucosidase inhibitor |
| | 0,837 | 0,004 | Anticarcinogenic | 0,713 | 0,002 | Beta-glucosidase inhibitor |
| | 0,833 | 0,004 | Manganese peroxidase inhibitor | 0,712 | 0,004 | D-threo-aldose 1-dehydrogenase inhibitor |
| | 0,837 | 0,012 | CYP2H substrate | 0,709 | 0,004 | Histamine release stimulant |
| | 0,827 | 0,002 | Licheninase inhibitor | 0,709 | 0,006 | Aspartyltransferase inhibitor |
| **catechin-[5,6-e]-4 b-(3,4-dihydroxyphenyl)dihydro-2(3H)-pyranone** | 0,934 | 0,005 | Membrane integrity agonist | 0,774 | 0,005 | Antihypercholesterolemic |
| | 0,924 | 0,004 | CYP1A1 substrate | 0,771 | 0,015 | Antineoplastic |
| | 0,910 | 0,005 | TP53 expression enhancer | 0,748 | 0,010 | Fibrinolytic |
| | 0,892 | 0,003 | UGT1A6 substrate | 0,743 | 0,006 | Hepatoprotectant |
| | 0,883 | 0,016 | CYP2C12 substrate | 0,731 | 0,002 | Astringent |
| | 0,864 | 0,003 | UGT1A substrate | 0,735 | 0,010 | Kinase inhibitor |
| | 0,857 | 0,005 | CYP1A substrate | 0,728 | 0,011 | CYP3A4 inducer |
| | 0,836 | 0,004 | UDP-glucuronosyltransferase substrate | 0,713 | 0,004 | Free radical scavenger |
| | 0,805 | 0,003 | Pectate lyase inhibitor | 0,711 | 0,005 | APOA1 expression enhancer |
| | 0,798 | 0,004 | Antimutagenic | 0,713 | 0,011 | CYP3A inducer |
| | 0,798 | 0,008 | CYP2B6 substrate | 0,705 | 0,006 | CYP2A11 substrate |
| | 0,787 | 0,004 | Lipid peroxidase inhibitor | 0,737 | 0,040 | Mucomembranous protector |
| | 0,780 | 0,004 | HMOX1 expression enhancer | 0,702 | 0,006 | CYP2A4 substrate |
| | 0,786 | 0,013 | HIF1A expression inhibitor | 0,706 | 0,014 | CYP3A5 substrate |
| | 0,775 | 0,004 | Chemopreventive | | | |
| **2-(6-benzoyl-bD-glucopyranosyloxy)-7-(1 a,2 a,6 a-trihydroxy-3-oxocyclohex-4-enoyl)-5-hydroxybenzyl alcohol** | 0,939 | 0,004 | Membrane integrity agonist | 0,829 | 0,014 | Alkenylglycerophosphocholine hydrolase inhibitor |
| | 0,933 | 0,005 | CDP-glycerol glycerophosphotransferase inhibitor | 0,821 | 0,009 | Antineoplastic |
| | 0,894 | 0,004 | Anaphylatoxin receptor antagonist | 0,810 | 0,005 | Antiinfective |
| | 0,874 | 0,004 | Membrane permeability inhibitor | 0,769 | 0,006 | Anticarcinogenic |
| | 0,854 | 0,003 | Monophenol monooxygenase inhibitor | 0,747 | 0,004 | H+-exporting ATPase inhibitor |
| | 0,851 | 0,010 | Benzoate-CoA ligase inhibitor | 0,744 | 0,011 | UDP-glucuronosyltransferase substrate |
| | 0,836 | 0,003 | Lactase inhibitor | 0,732 | 0,009 | Mucinaminylserine mucinaminidase inhibitor |
| | 0,842 | 0,011 | CYP2H substrate | 0,715 | 0,014 | Antiinflammatory |
| | 0,840 | 0,011 | Sugar-phosphatase inhibitor | 0,710 | 0,016 | Exoribonuclease II inhibitor |
| | 0,833 | 0,004 | 3-Phytase inhibitor | | | |
| **Chrysoeriol-7-O- b-D-glucopyranoside** | 0,982 | 0,001 | Monophenol monooxygenase inhibitor | 0,834 | 0,006 | NAD(P)+-arginine ADP-ribosyltransferase inhibitor |
| | 0,976 | 0,001 | Membrane permeability inhibitor | 0,829 | 0,005 | CYP3A inducer |
| | 0,976 | 0,002 | Membrane integrity agonist | 0,830 | 0,009 | Antineoplastic |
| | 0,974 | 0,001 | Cardioprotectant | 0,825 | 0,004 | UGT1A9 substrate |
| | 0,973 | 0,001 | Vasoprotector | 0,810 | 0,001 | Alpha glucosidase inhibitor |
| | 0,972 | 0,001 | Free radical scavenger | 0,821 | 0,013 | Sugar-phosphatase inhibitor |
| | 0,971 | 0,001 | Hemostatic | 0,818 | 0,017 | Chlordecone reductase inhibitor |
| | 0,959 | 0,000 | Beta-N-acetylhexosaminidase inhibitor | 0,807 | 0,006 | Membrane integrity antagonist |
| | 0,956 | 0,003 | TP53 expression enhancer | 0,803 | 0,003 | Antioxidant |
| | 0,951 | 0,002 | Chemopreventive | 0,795 | 0,001 | Skin whitener |
| | 0,948 | 0,002 | Hepatoprotectant | 0,793 | 0,002 | CYP2E1 inducer |
| | 0,945 | 0,002 | CYP1A inducer | 0,796 | 0,006 | Kinase inhibitor |
| | 0,943 | 0,002 | Anticarcinogenic | 0,792 | 0,003 | Mediator release inhibitor |
| | 0,943 | 0,002 | Lipid peroxidase inhibitor | 0,784 | 0,004 | 3-Phytase inhibitor |
| | 0,940 | 0,001 | NADPH oxidase inhibitor | 0,782 | 0,005 | Antiinfective |
| | 0,941 | 0,003 | Caspase 3 stimulant | 0,777 | 0,004 | UGT1A1 substrate |
| | 0,940 | 0,003 | Anaphylatoxin receptor antagonist | 0,767 | 0,002 | Caspase 8 stimulant |
| | 0,940 | 0,003 | UDP-glucuronosyltransferase substrate | 0,770 | 0,010 | Apoptosis agonist |

| | | | | | | |
|---|---|---|---|---|---|---|
| | 0,930 | 0,002 | Antiprotozoal (Leishmania) | 0,763 | 0,007 | Mucinaminylserine mucinaminidase inhibitor |
| | 0,929 | 0,005 | CDP-glycerol glycerophosphotransferase inhibitor | 0,754 | 0,002 | Sweetener |
| | 0,923 | 0,003 | Antihypercholesterolemic | 0,756 | 0,004 | Mycothiol-S-conjugate amidase inhibitor |
| | 0,920 | 0,001 | CYP1A1 inducer | 0,760 | 0,010 | 2-Dehydropantoate 2-reductase inhibitor |
| | 0,913 | 0,001 | 4-Coumarate-CoA ligase inhibitor | 0,772 | 0,022 | Alkenylglycerophosphocholine hydrolase inhibitor |
| | 0,895 | 0,001 | Histamine release stimulant | 0,743 | 0,005 | Cyclic AMP phosphodiesterase inhibitor |
| | 0,893 | 0,001 | CYP2C9 inducer | 0,745 | 0,010 | Oxidoreductase inhibitor |
| | 0,893 | 0,001 | Laxative | 0,736 | 0,006 | Vasodilator |
| | 0,892 | 0,000 | Capillary fragility treatment | 0,729 | 0,002 | Glucan 1,6-alpha-glucosidase inhibitor |
| | 0,897 | 0,006 | HIF1A expression inhibitor | 0,733 | 0,008 | Radioprotector |
| | 0,887 | 0,003 | UGT1A substrate | 0,750 | 0,026 | CYP2H substrate |
| | 0,881 | 0,001 | UGT1A7 substrate | 0,727 | 0,004 | Beta glucuronidase inhibitor |
| | 0,881 | 0,003 | Sulfotransferase substrate | 0,725 | 0,010 | Nucleotide metabolism regulator |
| | 0,874 | 0,002 | Proliferative diseases treatment | 0,719 | 0,005 | Antiviral (Influenza) |
| | 0,871 | 0,001 | Xanthine dehydrogenase inhibitor | 0,719 | 0,007 | Histidine kinase inhibitor |
| | 0,863 | 0,004 | CYP3A4 inducer | 0,715 | 0,004 | Choleretic |
| | 0,845 | 0,003 | Lactase inhibitor | 0,706 | 0,007 | HMOX1 expression enhancer |
| | 0,847 | 0,005 | Cytostatic | 0,707 | 0,009 | Antifungal |
| | 0,852 | 0,010 | Benzoate-CoA ligase inhibitor | 0,701 | 0,004 | Antitussive |
| | 0,833 | 0,001 | Aryl hydrocarbon receptor agonist | | | |
| **Mururin A** | 0,934 | 0,005 | Membrane integrity agonist | 0,808 | 0,006 | CYP1A substrate |
| | 0,925 | 0,004 | TP53 expression enhancer | 0,781 | 0,003 | Pectate lyase inhibitor |
| | 0,900 | 0,002 | Antimutagenic | 0,777 | 0,004 | CYP2A11 substrate |
| | 0,873 | 0,004 | UGT1A6 substrate | 0,777 | 0,004 | General pump inhibitor |
| | 0,861 | 0,003 | Histidine kinase inhibitor | 0,747 | 0,004 | Histamine release inhibitor |
| | 0,861 | 0,003 | UGT1A substrate | 0,745 | 0,005 | HMOX1 expression enhancer |
| | 0,861 | 0,004 | CYP1A1 substrate | 0,739 | 0,006 | Hepatoprotectant |
| | 0,843 | 0,003 | Chemopreventive | 0,731 | 0,004 | Free radical scavenger |
| | 0,841 | 0,004 | UDP-glucuronosyltransferase substrate | 0,730 | 0,004 | CYP1A inhibitor |
| | 0,841 | 0,008 | Antineoplastic | 0,726 | 0,005 | UGT1A1 substrate |
| | 0,855 | 0,023 | CYP2C12 substrate | 0,714 | 0,005 | Antineoplastic (breast cancer) |
| | 0,821 | 0,004 | Sulfotransferase substrate | 0,705 | 0,006 | CYP2A4 substrate |
| | 0,822 | 0,010 | HIF1A expression inhibitor | | | |

*probability of activity, # probability of inactivity

## Conclusion

The ethnobotanicals have been regularly used since the ancient civilization as ethnomedicine's for various illness from simple cold to threat full diseases like cancer etc., As recent report of WHO testifies that about 80% of the world's population relies on the phytopharmaceuticals for the treatment of various common diseases. In the era of many emerging and re-emerging diseases phytochemical compounds derived from plant sources have great pharmacological importance. The cure for a particular disease is addressed by a potent lead molecule for their biological activities against the disease therefore; computational approach has led to the identification of drug target and in the prediction of novel leads. In present study we have analyzed six isolated compounds from *Flacourtia indica* through QSAR approach computationally*;* it is interesting to reveal that all the six compounds were nontoxic and showing good ADMET profiles and high drug likeness properties with many biological activities and mechanism of actions. Screening of bioactive compounds from plants as source, has restored health benefits due to their biological activities, thus in the present study phytocompounds from *Flacoutia indica* provides ethnomedical evidences as potential phytopharmaceuticals, however further *In vitro* and *In vivo* analysis of each compound for various pharmacological benefits can be carried out for the discovery of novel drug compounds.

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