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Screening of Biological Activities through QSAR analysis of bioactive molecules of *Cardiospermum halicacabum*

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Abstract

Cardiospermum halicacabum, known as the balloon plant or love in a puff, is a climbing plant widely distributed across tropical and subtropical areas of Africa, Australia, and North America. In this current project, we have made an attempt to design computationally screening of compounds from *Cardiospermum halicacabum*. The 14phytoconstituents from the plant *cardiospermum halicacabum* were retrieved and screened for its Lipinski rule of 5 (Rule for oral drug molecules). Further Build QSAR studies were performed for 14 compounds to screen its Biological Activities. Computational QSAR is one of the most frequently used method in drug development, which provides quantitative information of a compound based on their biological properties by providing consequence of small molecules on its activity. QSAR studies revealed out of 14 compounds only 5 compounds lies on regression line of the graph (molecular weight versus molecular refractivity).The future studies could be designed accordingly to highlight the efficiency of the compounds Lutoline, Apoptosis, Kaemferol, Apigenin, Cardiospermin from the plant *Cardiospermum halicacabum* towards drug development process (*in vitro* and *in vivo*) for the safety usage of dose to the patients.

Keywords: *Cardiospermum halicacabum*, Phytochemicals, Lipinski rule of 5, Build QSAR.

Introduction

Plant-based medicines have long been used in traditional medicine to treat a variety of illnesses. 80 percent of the world's population still relies on medicinal plants for urgent health treatment, especially in areas where medications are unlikely to be available [Bachtel N *et al.,* 2020]. Plant-based bio-friendly and eco-friendly commodities have recently been explored for the prevention and treatment of various sorts of infections in humans, as well as microbial diseases, all over the world, and plant recruitment in ethnomedicine, among other advancements [Dias DA *et al.,* 2012]. Nature has lavished us with botanical riches, with a vast array of different plant kinds growing in various sections of the country [Walji R *et al.,*2009, Welz AN *et al.,*2018]. Herbal medications are now widely used in health-care initiatives in underdeveloped countries [Lee GB *et al.,*2004], India is rich in biodiversity on all three levels: species diversity, habitat diversity, and genetic diversity[Thomson P*et al.,*2014].Herbal medicine is still commonly utilised in developing nations by about 75-80% of the world's population[Sharma E *et al.,* 2017]. Plants include a variety of active biomolecules and phytochemicals that have an important role in the treatment of life-threatening disorders [Ghosh P*etal.,* 2018]. Several herbal plants have been studied in order to discover new substances and their mechanisms for preventing a variety of ailments[Pieroni A *et al.,*2012]. There are thousands of documented medicinal species in India, and the use of various portions of many medicinal plants to heal specific diseases has been in vogue since ancient times, and India is known as a land of herbal plants; thus, any specific data on such plants could be of clinical importance [Antony Reen a*et al.,*2011].

Many ailments have been cured using the various portions of a plant and their bioactive components as either food or medicine [Bhutani KK *et al.,*2010]. Understanding plant bioactive components and standardizations, as well as pharmacological activities such as in vivo and in vitro testing, through which drug quality, controlled toxicity, and adulterations can be disclosed in order to ensure customer safety and welfare [Ghosh P*et al.,* 2018]. The complex bioactive components and relatively abundant scopes in plants and its parts have been taken into account to separate the bioactive compounds, and research on this plant aids in the analysis of its toxicological and pharmacological activities for the implementation of new methodologies[Upadhyay RK*et al.,* 2015]. To treat a variety of disorders, the effectiveness, validity, and safety must be determined. As a result, human society can profit from usingherbal drug for their healthcare problems [Tyagi S*et al.,* 2015].

The Sapindaceae family includes Cardiospermumhalicacabum Linn. Balloon vine is its common name. Mudakkathan is a Tamil name. Annual climber stems are minutely puberulous and have tendrils [Vijayakumar N*et al.,* 2021]. Leaves are biternate, effectively trifoliate, with each section separated into three leaflets, each with coarse serrate teeth. Abortion produces three-flowered flowers in the axillary heads, which are white with a yellowish core. Green, membranous, inflated capsule that dries to brown and is over 2 cm long. Seeds with a broad heart-shaped or kidney-shaped spot are round and black [Bruno J Neves *et al.,* 2018, Zalke AS*et al.,* 2013].

This plant is widely distributed throughout the world's tropical and subtropical regions. The plains of Africa, America, Bangladesh, India, and Pakistan yield this plant [Uma AnushaNukala*et al.,* 2015, Senthilkumar S*et al.,* 2012]. Previous studies that reported phytochemical investigations of the plant revealed that extracts of this plant had antibacterial [Viji M*et al.,*2010], antifungal [Jeyadevi R*et al.,*2013], antiparasitic [Boonmars T*et al.,*2005], antidiarrheal [Prakash KC*et al.,*2014], anxiolytic [Mahmood R*et al.,*2016], antidiabetic [Govindappa M 2015], antiarthritic [Padmini N*et al.,*2016], anti-inflammatory [Huang MH*et al.,*2011], anticonvulsant, and anticarcinogenic [Rajesh S*et al.,*2016],

neuroprotective role [Kukkar MR*et al.*,2014]properties due to the presence of various chemical constituents.

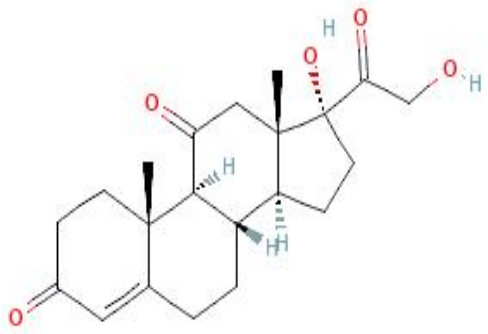
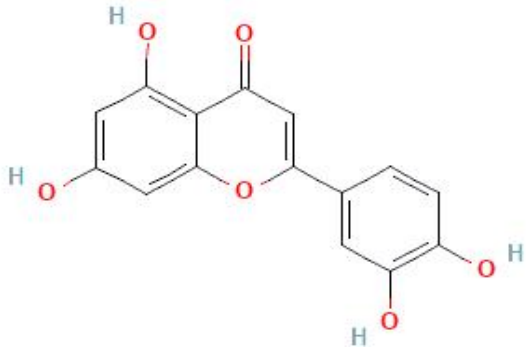
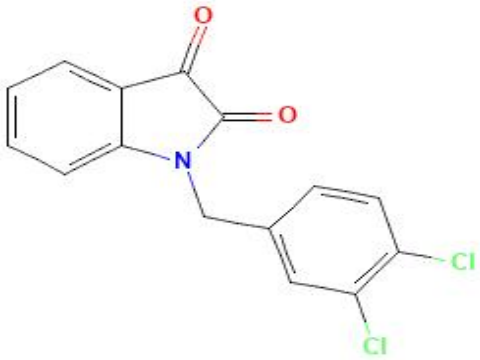
Hence we put forth importance towards the organic natural compounds obtained easily from plants without any side effects. The compounds from the plant *Cardiospermum halicacabum* are virtually screened for drug-likeness using the Molinspiration Server. The drug compounds are subjected for QSAR analysis. QSAR(Quantitative Structure-Activity Relationship)are mathematical relationships linking chemical structure and pharmacological activity in a quantitative manner for a series of compounds [Sarkar S*et al.*,2020]. Methods which can be used in QSAR include various regression and pattern recognition techniques, usually done by BuildQSAR software [Mohammad Goodarzi *et al.*,2012]. The aim of the current study was to predict the novel biomolecules with fewer side effects from the plant *Cardiospermum halicacabum to* treat various diseases.

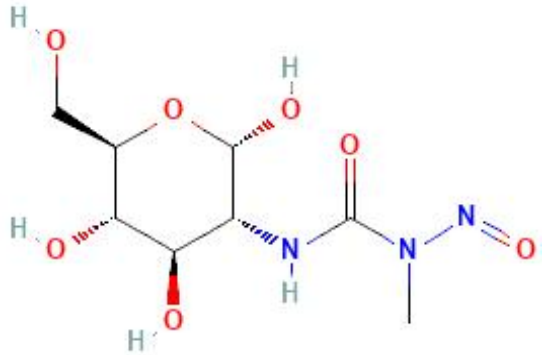
Materials and Methods

Preparing models for QSAR analysis:

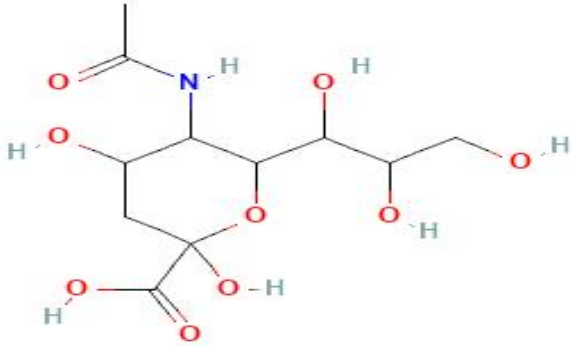
From the plant *Cardiospermum halicacabum* totally 14 compounds were identified from the various literatures (Table 1).The evaluations of the drug were performed by Molinspiration server (www.molinspiration.com).The server evaluates the compound's drug likeness using the Lipinski's Rule which confirms the property of an oral drug for 14 compounds.

Table 1: 2D structure of plant compounds of *Cardiospermum halicacabum* along with its Pubchem ID

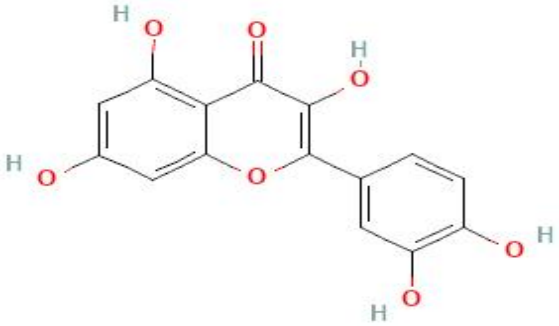
 Cortisone, Pubchem ID: 222786	 Luteolin, Pubchem ID:5280445
 1-Methyl-3-(1-methyl-1H-indol-3-yl)-4-(pentylamino)-1H-pyrrole-2,5-dione Pubchem ID: 16760577	 Apoptosis, Pubchem ID: 1901244



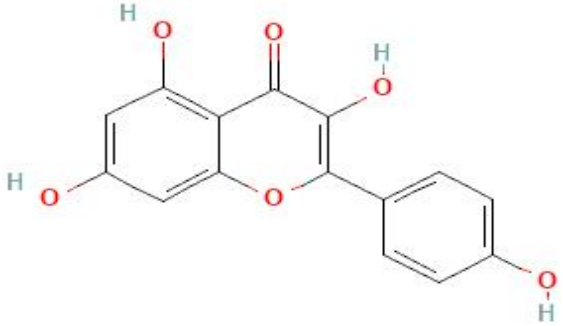
Streptozocin, Pubchem ID: 29327



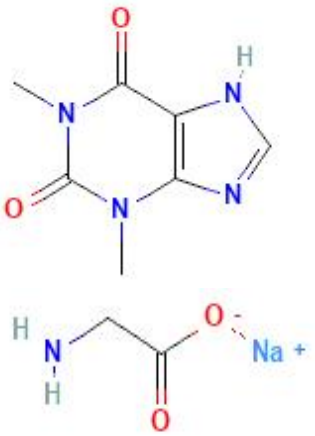
Sialic acid, Pubchem ID: 906



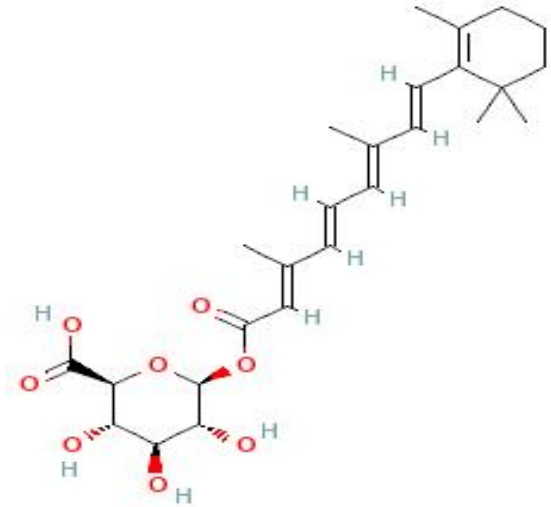
Quercetin, Pubchem ID: 5280343



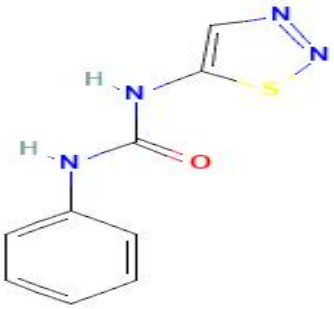
Kaempferol, Pubchem ID: 5280863



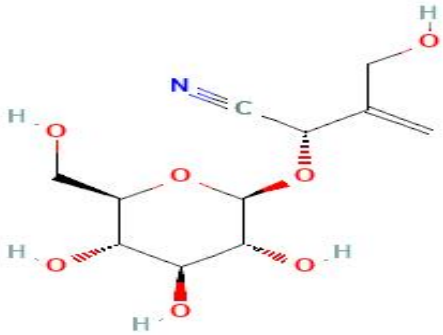
Theophylline Sodium Glycinate, Pubchem ID:23663537



Retinoyl beta-glucuronide, Pubchem ID:5281877

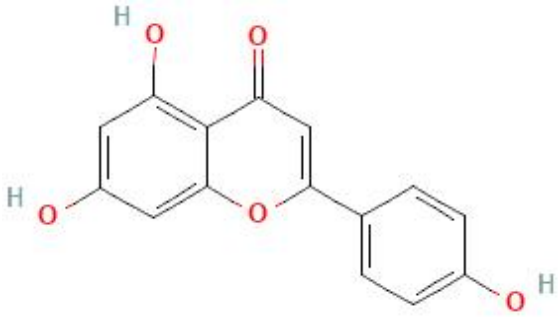


Thidiazuron, Pubchem ID:40087



Cardiospermin, Pubchem ID:179647

Carbamazepine, Pubchem ID:2554



Apigenin, Pubchem ID:5280443

Building QSAR Models

QSAR analysis is performed on the expected values for the dataset of 14 pharmacological molecules. To determine the optimum drug to suppress the activity of receptor protein, the activity (MolWt) is linked to the descriptors. The Molecular Weight values are used as the activity (dependent variable) and compared to the descriptors (TPSA, number of H-bond donors, number of H-bond acceptors) to create a dataset. Different QSAR plots are now created by linking activity to various descriptors (independent variables). Finally, one activity was plotted against each description in each graph.

The compounds are shown in a graph using the Build QSAR software to forecast the optimal compound. The Y-axis represents the dependent variable, while the X-axis represents the independent variables. The regression line (diagonal line) is obtained after more charting, and a specific number of compounds are visible on the fit line. The molecules detected on the line are more closely related to descriptors indicating a drug's effectiveness.

Results and Discussion

Figure 1 : Descriptors of QSAR

BuildQSAR

File Edit View Dataset QSAR Tools Windows Help

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	ID	Structure	molecular weight	hydrogen bond donor	hydrogen bond acceptors	logP	molecular refractivity
1	C-01	222786	360.0	1.0	5.0	3.0	101.0
2	C-02	5280445	286.0	4.0	6.0	0.0	63.0
3	C-03	16760577	325.0	1.0	2.0	2.0	92.0
4	C-04	1901244	306.0	0.0	2.0	3.0	70.0
5	C-05	29327	265.0	5.0	7.0	0.0	52.0
6	C-06	906	309.0	6.0	9.0	0.0	65.0
7	C-07	5280343	302.0	5.0	7.0	0.0	64.0
8	C-08	5280863	286.0	4.0	6.0	0.0	62.0
9	C-09	5280443	270.0	3.0	5.0	0.0	61.0
10	C-10	5281877	476.0	4.0	8.0	4.0	129.0
11	C-11	40087	220.0	2.0	1.0	0.0	47.0
12	C-12	179647	275.0	5.0	8.0	0.0	64.0
13	C-13	2554	236.0	1.0	1.0	1.0	63.0
14	C-14	23663537	277.0	3.0	4.0	-0.0	52.0

QSAR Model's Graph analysis:

The Molinspiration server is used to estimate the dependent and independent factors for all phytocompounds. The activities and descriptors of medicinal compounds from figure 1 are manually entered into the BuildQSAR software and various graphs between the dependent variable (MolWt) and the other independent variables are plotted (TPSA, H-bond acceptors and H-bond donors). Every graphical analysis found a link between them.

QSAR model development:

To determine the optimal compound, the various models were built by correlating the independent factors (Descriptors) and dependent variables (MolWt). Finally, by comparing each graph derived from the QSAR plot, the best compounds with pharmacological activity plotted between MolWt and structural descriptors that fit in the regression line are identified. Drug activity is measured along the Y-axis, and descriptors are measured along the X-axis, to create graphical models for the best fit compounds. The graph shows that compounds that fit in the regression line (diagonal line) and are close to the line have a high correlation and are thus likely to have therapeutic action against macromolecules.

Figure 2 :Graph was plotted between Molecular Weight &Hydrogen bond donor

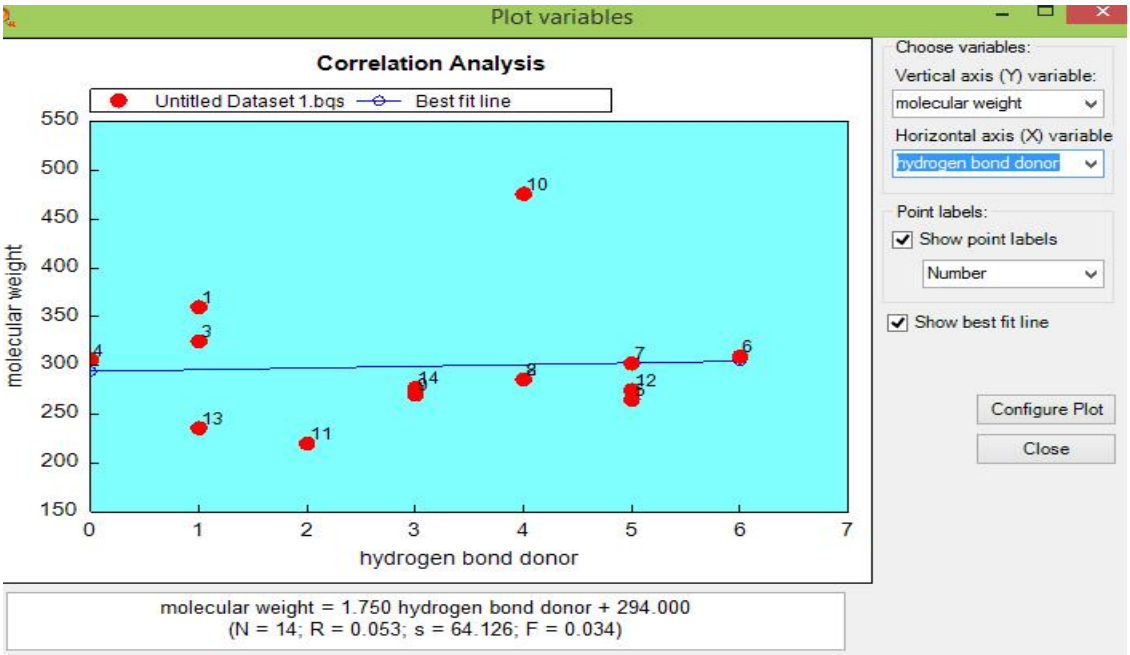


Figure 3 :Graph was plotted between Molecular Weight &LogP

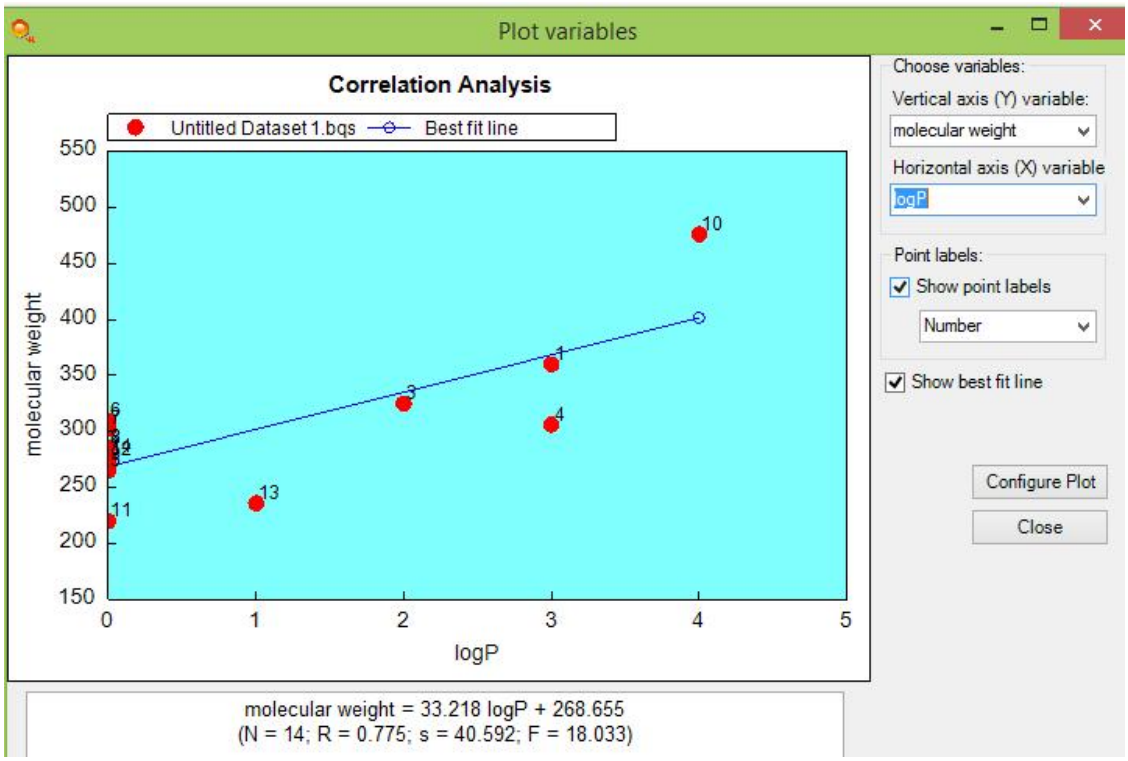


Figure 4 :Graph was plotted between Molecular Weight &Hydrogen bond acceptor

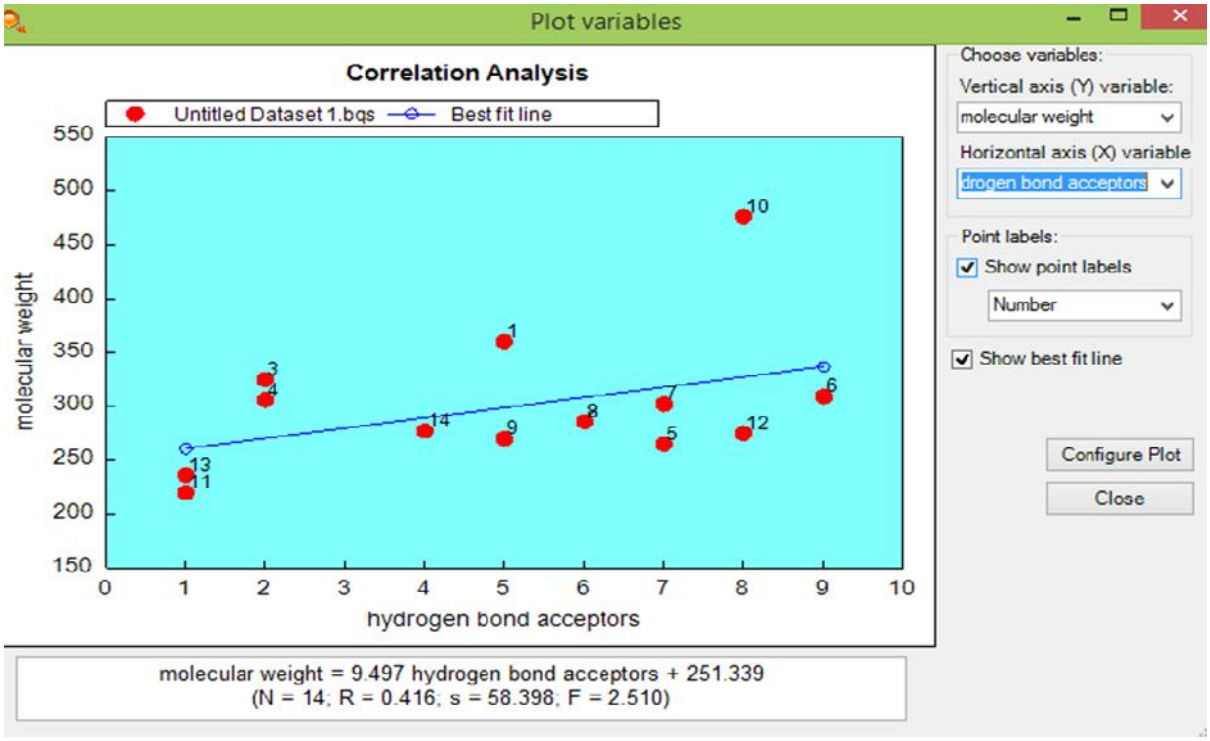
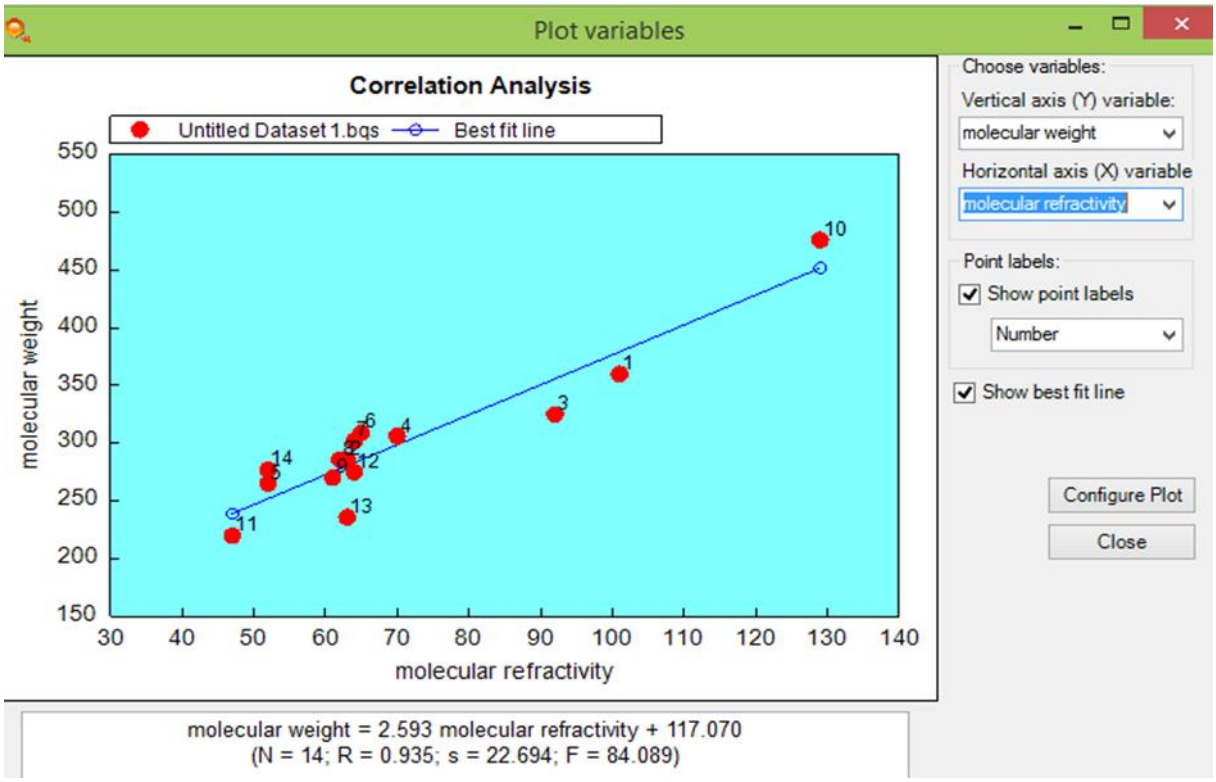


Figure 5 :Graph was plotted between Molecular Weight &Molecular Refractivity



From the figure 2 it was predicted that the 3 Compounds fits in the regression line between Molecular Weight and Hydrogen bond donorwith the R value 0.053. The compounds were as follows:

- The position 7 represent the Quercetin compound with the pubchem ID 5280343
- The position 6 represent the Sialic acid compound with the pubchem ID 906
- The position 4 represent the Apoptosis compounds with the pubchem ID 1901244

From the figure 3 it was predicted that the 3 Compounds fits in the regression line between Molecular Weight andLogP with the R value 0.775. The compounds were as follows:

- The position 5 represent the Streptozocin compound with the pubchem ID 29327
- The position 3 represent the Necrosis compound with the pubchem ID 16760577
- The position 1 represent the Cortisone compound with the pubchem ID 222786

From the figure 4 it was predicted that the no Compounds fits in the regression line between Molecular Weight and Hydrogen bond acceptor with the R value 0.416.

From the figure 5 it was predicted that the 5 Compounds fits in the regression line between Molecular Weight and Molecular Refractivity with the R value 0.935. The compounds were as follows:

- The position 2 represent the Luteolincompound with the pubchem ID 5280343
- The position 4 represent the Apoptosis compound with the pubchem ID 906
- The position 8 represent the Kaempferolcompound with the pubchem ID 1901244
- The position 9 represent the Apigenin compound with the pubchem ID 906
- The position 12 represent the Cardiospermincompound with the pubchem ID 1901244

On analysing R value in Build QSAR result, it was clearly revealed that the 5 compounds (Lutoline, Apoptosis, Kaemferol, Apigenin, Cardiospermin) which was predicted between descriptors of Molecular Weight and Molecular Refractivity was expected to exhibit the better inhibitory activity towards target protein when compared with other compounds.

Conclusion

A plant of enormous importance to society as a whole and further research into its therapeutic capabilities and phytochemical studies could improve this herb's future prospects as a life-saving plant. So in this study on plant compounds *Cardiospermum halicacabum* using Build QSAR generated four different QSAR models were built based on the descriptors,. Only 5 compounds out of 14 are found on the graph's regression line, according to QSAR research (molecular weight versus molecular refractivity). Future research might be tailored to demonstrate the efficacy of Lutoline, Apoptosis, Kaemferol, Apigenin, and Cardiospermin components from the plant *Cardiospermum halicacabum* in the medication development process .The results of the current work could be employed to generate new ligand molecules, determine their activities in Insilco, and prove that they are consistent with experimental values. As a result, the findings can be applied to the rational medication design of novel and potent lethal factor inhibitors.

Conflict of interest:

The authors declare they have no competing interests.

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