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Original Article

IN SILICO STUDIES OF THE SECONDARY METABOLITES OF *SOLANUM TORVUM* SW. FOR THEIR ANTIASTHMATIC ACTIVITY

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ABSTRACT

Objective: *Solanum torvum* Sw., Family: Solanaceae, commonly known as Turkey Berry is used by the traditional tribes for the treatment of cold, cough, tuberculosis, hepatotoxicity, cancer, etc. The action of the plant towards the treatment of these diseases has been proven except for asthma. The present study is to prove the antiasthmatic activity of methanolic extract and the secondary metabolites of *Solanum torvum* Sw using *in silico* docking studies in compare to reference standard Dexamethasone, a synthetic cortisone derivative.

Methods: The GC-MS analysis of the dried methanolic extract of the dried fruits of *Solanum torvum* Sw. and the total saponin fraction has been carried out to know the important moieties that are responsible for the antiasthmatic activity.

Results: The results from the docking studies showed that the compounds Cholesta-5,7,9-(11)-trien-3-ol,4,4-dimethyl, (3á); Lanosta-7,9-(11),20-triene-3α, 18-diol, diacetate and Cholestan-26-oic acid,3,7,12,24-tetrakis (acetyloxy), methyl ester, (3à,5á,7à,12à) were found to have significant scores of-6.8,-6.9 and-6.9 respectively towards Glucocorticoid receptor protein (Gr), (PDB id: 4UDC) which is very similar to the affinity of the standard (-7.1). These compounds passed the drug-likeness test. A modification in the structure can be brought, which makes the compounds more potent. The compounds 9, 12-Octadecadienoic acid, ethyl ester; Hexadecanoic acid, ethyl ester; 9-Octadecenoic acid (Z), methyl ester; Oxacycloheptadec-8-en-2-one, (8Z) have passed the Blood Brain Barrier (BBB) filter of the drug-likeness test.

Conclusion: The antiasthmatic activity of the drug may be due to the similarity with the structure of Dexamethasone. Further research can be carried out in order to improve the clinical significance of these extracts and its metabolites.

Keywords: Solanum torvum Sw., Traditional tribes, Antiasthmatic activity, GC-MS analysis, *in silico* docking studies, Drug-likeness test

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INTRODUCTION

Traditional medicine is "the knowledge, skills and practices based on the theories, beliefs and experiences indigenous to different cultures, used in the maintenance of health and in the prevention, diagnosis, improvement or treatment of physical and mental illness" [1]. The main aim of traditional medicine is to use the resources available from the nature for the treatment of diseases and to maintain the goodness of life.

The Solanaceae or the nightshades are an economically important family of flowering plants. The family ranges from annual and perennial herbs to vines, lianas, epiphytes, shrubs and trees. An important genus of the family is Solanum. This genus consists of a number of medicinal plants which contains unique alkaloids and are medicinally important [2].

Solanum torvum Sw. (Family: Solanaceae), commonly known as Turkey Berry [3] is native to Mexico, Peru and Venezuela. It is widely distributed in Africa, West Indies, India, Bermuda, Indonesia, Malaya, China, Philippines and tropical America [4]. It is used in the folk and traditional medicine for treatment of diseases like asthma, diabetes, gastrointestinal diseases etc. The researches done on *Solanum torvum* had shown that the plant possesses significant antimicrobial, anticancer, diuretic, anti-inflammatory, anti-influenza activity [5]. The use of the plant to treat asthma by the traditional people is not yet scientifically validated.

Asthma is a common long-term inflammatory disease of the airways of the lungs [6]. It is characterized by recurring symptoms like wheezing, coughing, chest tightness and shortness of breath. These symptoms are due to the reversible airflow obstruction and bronchospasm [7].

Asthma is the result of chronic inflammation of the conducting zone of the airways which result in increased contractibility of the surrounding smooth muscles.

The beneficial effects of glucocorticoids in asthmatic patients were first described in 1950 [8]. Many studies have focused on the therapeutic potential of glucocorticoids. Several synthetic glucocorticoids which are more potent than cortisol without mineralocorticoid side effects have been developed. Nowadays, glucocorticoids are powerful agents in the treatment of inflammatory diseases, allergic conditions and asthma [9].

The effects of inhaled glucocorticoids on bronchial inflammation are studied either by measurements in Bronchoalveolar lavage fluid (BALF), sputum, exhaled air or by performing bronchial biopsies. These studies have confirmed that glucocorticoid treatment of asthmatic patients reduces the number and activation of inflammatory cells in the airways, together with an improvement of lung function. The potent anti-inflammatory actions of glucocorticoids are thought to underlie the clinical efficacy of oral glucocorticoids [10].

Effects of glucocorticoids on lung function

Treatment with glucocorticoids has been consistently shown not only to reduce the symptoms of asthma but also bronchial hyper responsiveness [11]. In contrast to the rapid inhibitory effects of β_2-agonists, glucocorticoids given in a single dose are not effective in preventing early allergen-invoked bronchoconstriction, but inhibition of the late response has been clearly demonstrated [12]. The inhaled glucocorticoids consistently reduce airway hyper-reactivity in asthmatics [13], but even after several months of treatment responsiveness fails to return to the normal range. This may reflect the persistence of structural changes that can not be reversed by steroids such as the thickening of the basement membrane, despite of suppression of the inflammatory and immunological processes.

The glucocorticoids act by inhibiting the following actions: [9]

1. T-cell activation
2. Cytokine production
3. Mast cell mediator release
4. Eosinophil mediator release

The synthetic derivatives of glucocorticoid which are used for the treatment of asthma include Dexamethasone, a cortisol derivative and a glucocorticoid agonist [14]. In the present study, Dexamethasone is taken as standard.

The present study aims at proving the antiasthmatic activity of the compounds interpreted in the methanolic extract of the dried fruits *Solanum torvum* Sw and the saponin fraction of the methanolic extract through *in silico* docking studies.

MATERIALS AND METHODS

Collection and authentication of plant material

The fruits of *Solanum torvum* Sw. were collected from the tribal village, Thukkanaikanpalayam, Erode, TN and authenticated by the Professor, Department of Herbal plant cultivation, Tamilnadu Agricultural University, Coimbatore.

Extraction of plant material

The shade dried fruits of *Solanum torvum* Sw. were powdered and dried at 40˚C in the hot air oven. The dried powder was extracted in Soxhelet apparatus by continuous hot percolation using 70% methanol as solvent. After 15-20 syphons the solvent was distilled to obtain the crude extract. The weight of the crude extract was taken and the yield was calculated. This crude extract was used for the further analysis.

Isolation of compounds

100g of the methanolic extract of the dried fruits of *Solanum torvum* Sw. was refluxed with petroleum ether, chloroform, ethyl acetate and n-butanol individually for one hour. As per the literature survey the saponin which is present in the Solanum species are fractionated with the help of n-butanol, was filtered and the filtrate was distilled. The filtrate produces a precipitate which is again filtered and the filtrate was evaporated to obtain the saponins. This saponin fraction was further analyzed.

Phytochemical screening

The qualitative phytochemical tests of the dried methanolic extract of the dried fruits of *Solanum torvum* Sw. was screened by the method described in Harborne, J. B.1973 [15].

GC-MS analysis

The compounds interpreted from the GC-MS analysis of the methanolic extract of the dried fruits *Solanum torvum* Sw and the saponin fraction of the extract are given in table 1 and 2.

In silico docking studies: [16]

AutoDock is a molecular modelling simulation software. It is especially effective for the protein-ligand docking. The compounds obtained were studied through docking to evaluate their antiasthmatic activity. In the present study, Dexamethasone was taken as standard and the glucocorticoid (Gr) is the target. The results of docking are given in table 3.

Drug-likeness

The compounds 9,12-Octadecadienoic acid, ethyl ester; Hexadecanoic acid, ethyl ester; 9-Octadecenoic acid (Z), methyl ester; Oxacycloheptadec-8-en-2-one,(8Z); Cholesta-5,7-dien-3-ol,4,4-dimethyl, (3á); Cholesta-5,7,9-(11)-trien-3-ol,4,4-dimethyl, (3á); Lanosta-7,9-(11),20-triene-3α, 18-diol, diacetate and Cholestan-26-oic acid,3,7,12,24-tetrakis (acetyloxy), methyl ester, (3à,5á,7à,12à) were tested for the drug-likeness through the DruLiTo software. The DruLiTo is a software which uses the structure of the compound as input and checks for the filters like Lipinski filter, Ghose filter, CMC-50 like the rule, Veber filter, MDDR-like filter, BBB likeness, Unweighted QED and weighted QED. The compound which passes these filters is eligible to be used as a drug.

RESULTS AND DISCUSSION

Macroscopic evaluation

The macroscopic evidence of the plant *Solanum torvum* Sw are as follows.

Fig. 1: *Solanum torvum* Sw

Fruits-The fruits are berries that are yellow when fully ripe. They are thin-fleshed and contain numerous flat, round, brown seeds.

Seeds-Seeds numerous, drab brownish, flattened, discoid, 1.5-2 mm long slightly reticulate, Self-compatible.

Odour-Pepper-like

Taste-Bitter and acrid

Phytochemical screening

The phytochemical analysis of the methanolic extract of the fruits of *Solanum torvum* Swartz was performed and the results showed the presence of

1. carbohydrate non-reducing sugars
2. steroids
3. flavonoids
4. glycosides including cardiac glycosides
5. alkaloids
6. saponins

GC-MS analysis

The compounds interpreted from the GC-MS analysis of the methanolic extract of the dried fruits *Solanum torvum* Sw and the saponin fraction of the extract are given in the table 1 and 2.

Table 1: The compounds interpreted from the dried methanolic extract of the dried fruits of *Solanum torvum* Sw

S. No.	Rt	Compound name	Molecular Formula	CAS No
1.	15.41	p-Xylenolphthalein	C24H22O4	50984-88-8
2.	16.36	Cholestan-26-oic acid,3,7,12,24-tetrakis (acetyloxy), methyl ester, (3α,5α,7α,12α)	C36H56O10	60354-51-0
3.	17.97	Lanosta-7,9-(11),20-triene-3α, 18-diol, diacetate	C34H52O4	24041-73-4
4.	18.57	Cholesta-5,7-dien-3-ol, 4,4dimethyl, (3α)	C29H48O	53296-71-2
5.	18.72	Cholesta5,7,9(11)trien-3-ol, 4,4dimethyl, (3α)	C29H46O	53296-72-3

Table 2: The compounds interpreted from the saponin fraction of the methanolic extract of the dried fruits of *Solanum torvum* Sw

S. No.	Rt	Compound	Molecular formula	CAS No
1.	16.17	p-Xylenolphthalein	C24H22O4	50984-88-8
2.	18.18	Hexadecanoic acid, ethyl ester	C18H36O2	628-97-7
3.	19.10	Cholesta-5,7,9-(11)-trien-3-ol,4,4-dimethyl,(3á)	C29H46O	53296-72-3
4.	20.03	9-Octadecenoicacid (Z), methyl ester	C19H36O2	112-62-9
5.	20.22	9,12-Octadecadienoicacid, ethyl ester	C20H36O2	7619-08-1
6.	20.39	Oxacycloheptadec-8-en-2-one,(8Z)	C16H28O2	123-69-3
7.	20.66	Cholesta-5,7-dien-3-ol,4,4-dimethyl,(3á)	C29H48O	53296-71-2
8.	33.66	Cholestan-26-oicacid,3,7,12,24-tetrakis (acetyloxy), methyl ester, (3à,5á,7à,12à)	C36H56O10	60354-51-0

Table 3 showing the affinity of the compounds obtained from the dried methanolic extract of the dried fruits of *Solanum torvum* Sw. and the saponin fraction of the extract towards the target

S. No.	Compound name	Affinity towards Glucocorticoid receptor (Gr)
1.	Dexamethasone	-7.1
2.	9,12-Octadecadienoic acid, ethyl ester	-3.0
3.	Hexadecanoic acid, ethyl ester	-3.2
4.	9-Octadecenoic acid (Z), methyl ester	-2.7
5.	Oxacycloheptadec-8-en-2-one,(8Z)	-6.5
6.	Cholesta-5,7-dien-3-ol,4,4-dimethyl,(3á)	-6.0
7.	Cholesta-5,7,9-(11)-trien-3-ol,4,4-dimethyl,(3á)	-6.8
8.	Lanosta-7,9-(11),20-triene-3α, 18-diol, diacetate	-6.9
9.	Cholestan-26-oicacid,3,7,12,24-tetrakis (acetyloxy), methyl ester, (3à,5á,7à,12à)	-6.9

In vitro docking studies

The standard Dexamethasone was found to have the affinity of-7.1 towards Gr. The compounds Cholesta-5,7,9-(11)-trien-3-ol,4,4-dimethyl, (3á); Lanosta-7,9-(11),20-triene-3α, 18-diol, diacetate and Cholestan-26-oic acid,3,7,12,24-tetrakis (acetyloxy), methyl ester, (3à,5á,7à,12à) are found to have the affinity of-6.8,-6.9 and-6.9 towards Gr which is very similar to the affinity of the standard which is shown in the fig. 2,3,4 and 5.

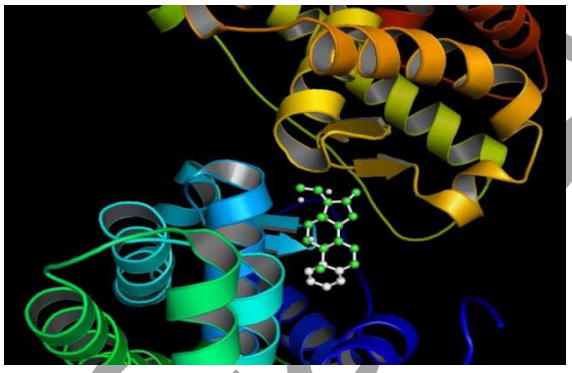

Fig. 2: Docking result of Dexamethasone with Gr

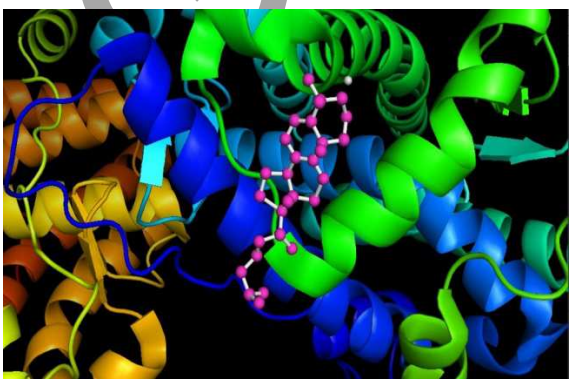

Fig. 3: Docking result of Cholesta-5,7,9-(11)-trien-3-ol,4,4-dimethyl, (3á) with Gr

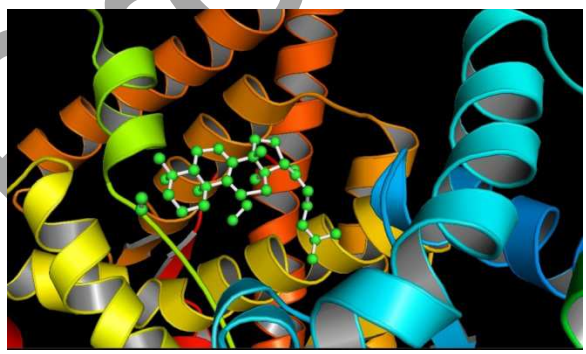

Fig. 4: Docking result of Lanosta-7,9-(11), 20-triene-3α, 18-diol, diacetate with Gr

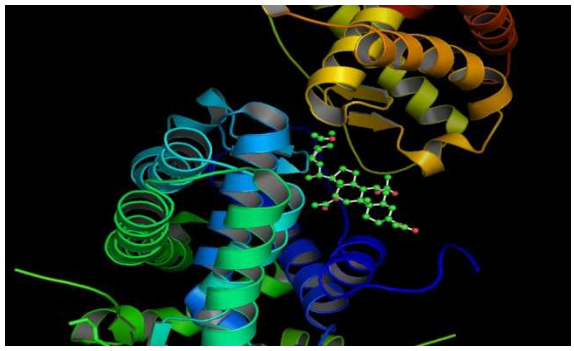

Fig. 5: Docking result of Cholestan-26-oic acid, 3,7,12,24-tetrakis (acetyloxy), methyl ester, (3à,5á,7à,12à) with Gr

Drug-likeness

The compounds 9,12-Octadecadienoic acid, ethyl ester; Hexadecanoic acid, ethyl ester; 9-Octadecenoic acid (Z), methyl ester; Oxacycloheptadec-8-en-2-one,(8Z); Cholesta-5,7-dien-3-ol,4,4-dimethyl,(3á); Cholesta-5,7,9-(11)-trien-3-ol,4,4-dimethyl, (3á); Lanosta-7,9-(11),20-triene-3α, 18-diol, diacetate and Cholestan-26-oic acid,3,7,12,24-tetrakis (acetyloxy), methyl ester, (3à,5á,7à,12à) were tested for the drug-likeness through the

DruLiTo software. The compounds pass the filters which indicate that the drugs are eligible to be used as drugs. A modification in the structure can be brought in the compounds which makes the compounds more potent.

The compounds 9,12-Octadecadienoic acid, ethyl ester; Hexadecanoic acid, ethyl ester; 9-Octadecenoic acid (Z), methyl ester; Oxacycloheptadec-8-en-2-one,(8Z) has passes the BBB filter.

CONCLUSION

The plant *Solanum torvum* Sw was named in 1964. But it is used as a vegetable in our routine diet from the time of our ancestors and also used for the treatment of various diseases including asthma. From the docking and drug likeness study, the results shown are

1. The compounds Cholesta-5,7,9-(11)-trien-3-ol,4,4-dimethyl, (3á); Lanosta-7,9-(11),20-triene-3α, 18-diol, diacetate and Cholestan-26-oic acid,3,7,12,24-tetrakis (acetyloxy), methyl ester, (3à,5á,7à,12à) are found to have the affinity of-6.8,-6.9 and-6.9 towards Gr which is very similar to the affinity of the standard (-7.1). These compounds have passed the drug-likeness test.

2. The compounds 9,12-Octadecadienoic acid, ethyl ester; Hexadecanoic acid, ethyl ester; 9-Octadecenoic acid (Z), methyl ester; Oxacycloheptadec-8-en-2-one,(8Z) have passed the BBB filter.

The present study revealed that the compounds obtained are therapeutically significant and also can be made more potent by further study in the structure activity relationship of the compounds. This study can also be taken as the first step of the research on the antiasthmatic activity of *Solanum torvum* Sw.

CONFLICT OF INTERESTS

Declare none

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