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Hepatoprotective Molecules and Extracts Profile from *Calotropis procera* R. Br.

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ABSTRACT

Plants have a great value as the source of medicine. They are most utilized in ayurveda medicine of system for the treatment of various ailments without and/or less adverse effect. *Calotropisprocera* is shrubby medicinal plant that evenly grows in the various parts of India as well as in other countries. Leaves, flower, stem, bark, root and latex of *Calotropisprocera*is used traditionally as bitter, laxative, anthelmintic, appetizer, stomachic, anti-sialagogue and strengthening. Scientist explored the various parts of *Calotropisprocera* for different pharmacological activities like anthelmintic, antidiarrhoeal, hepatoprotective,schizonticidal, wound healing and jaundice. The plant is explored up to the chemical level and various chemicals are isolated from the different parts of the plants such as calotropagenin, lupeol, α-amyrin, *β*-sitosterol, quercetin and rutin etc. This review was attempted to explore the hepatoprotective potential of extracts and chemical moiety obtained from the different parts of *Calotropisprocera*.

Keywords: *Calotropisprocera,* hepatoprotective, chemical constituents,calotropagenin, *α*-amyrin,rutin

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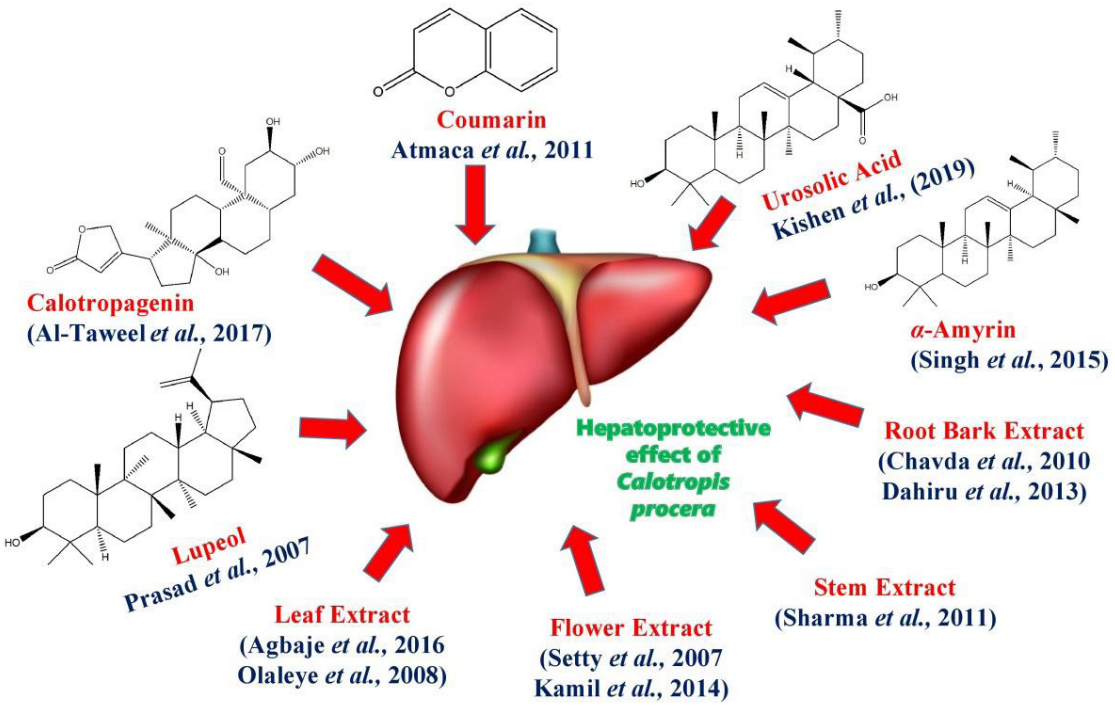
GRAPHICAL ABSTRACT



INTRODUCTION

India has an antiquated legacy of customary medication. Materiamedica of India gives bunches of data on the fables rehearses and customary part of restoratively significant characteristic items. Indian customary medication depends on different frameworks including Ayurveda, Siddha and Unani. The assessment of these medications isdependent on phytochemical, pharmacological and

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Calotropis procera R. Br. with Hepatoprotective Activity

methodologies including different instrumental techniques like chromatography, UV-spectroscopy, Mass spectroscopy, NMR and others. With the rising enthusiasm for the world to embrace and study the conventional framework are dependent on the distinctive human services frameworks, the assessment of the rich legacy of the customary medication is fundamental. The World Health Organization (WHO) appraises that about 80% of the populace living in the creating nations depends solely on customary medication for their essential human service'sneeds.[1]

Natural prescriptions are set up from an assortment of plant materials like leaves, stems, roots, bark, etc. Plants are viewed as restorative in the event that they have pharmacological exercises of conceivable helpful use. They contain numerous organically dynamic fixings and are utilized fundamentally for rewarding mellow or ceaseless afflictions.[2]

Traditionally the *Calotropisprocera*is used as bitter, laxative and anthelmintic. The flower is used as tonic, appetizer, stomachic, anti-sialagogue and strengthening. It is also used as toothache (fresh root), cholera (flower), infanticide (fresh milk), poultice (leaves), and headache (leaves). The leaves are used in the treatment of severe case of dyspepsia, constipation and mucus in stool.[3] *Calotropisprocera* have experimentally proved in numerous pharmacological activities like anthelmintic,[4,5] anti-diarrhoeal,[6] anti-fertility,[7] wound healing,[8] anti-microbial,[9] anti-nociceptive,[10] antioxidant,[11] anticonvulsant,[12] schizonticidal[13] analgesic,[14] diuretic,[15] cytotoxic[16] and anti-depressenat.[17]

Pharmacognostic Description

Calotropisprocera is an erectile shrub of height 1.8 to 2.4 m (except in dry places where it may grow higher form usual height). The leaves of *Calotropisprocera* have small stalk (subsessile), broadly ovate, ovate-oblong, elliptic with short abrupt acumination and glabrous. The bark is soft, corky and spongy and covered with cottony tomentum. The flower is umbellate cymes, glabrous, peduncles (2.5-7.5cm long), pedicels (6mm), buds globose, sepals (5-2.5mm), ovate, acute, corolla is glabrous (2.5cm), lobes are erect, ovate, acute and ovate (1cm) long. The apex is obliquely truncate, bifid, without auricles. The seeds are broadly ovate, acute, flattened, narrowly margined, minutely tomentose, light brown and 6-4mm in size.[18-22]

Chemical Constituents

Calotropisprocera has various types of biomolecules as their active chemical moieties like cardiac glycosides, terpines, flavanoids etc. as shown below. The various components of the plant used to treat various ailments in traditional medicine, and their result have been scientifically proven by experiments with the molecules involved in these studies.[23]

Cardenolides: Calotroposides,[24-27] Calotropin,[28-32] Calotropagenin,[33-35] Calotoxin,[36,37] Calactin,[38-40] Uscharin,[41] Proceraside A,[42-44] 3-epi-12β-hydroxyfroside, Coroglaucigenin (CGN).[45,46]

Terpenoids: Calotropursenyl acetate,[47] Calotropisis,[48] Lupeol,[49] α-Amyrin,[50] β-Amyrin,[51] Taraxasterol,[52] Calotroprocerone A,[53] Calotroproceryl acetate A,[54] Calotroproceryl acetate B,[55] Calotroprocerol A,[56] Pseudotaraxasterol acetate.[57]

Lignans: (+)-Pinoresinol 4-*O*-[6"-*O*-vanilloyl]-*β*-*D*-glucopyranoside, 9'-methoxypinoresinol, (+)-pinoresinol 4-*O*-*β*-*D*-glucopyranoside, (+) medioresinol 4-*O*-*β*-*D*-glucopyranoside, (+)-pinoresinol 4-*O* [6"-*O*vanillyl]- *β*-*D*-glucopyranoside, (+)-pinoresinol 4-*O*-[6"-*O*protocatechuoyl]-*β*-*D*-glucopyranoside, Pinoresinol-4'-*O*-[6"-*O*-(*E*)-feruloyl]-*β*-*D* glucopyranoside.[58-60]

Sterols:*β-Sitosterol,* urs-19(29)-en-3-yl acetate, Multiflorenol,Urs-19(29)-en-3-β-ol,3β,27-dihydroxy-urs-18-en-13,28-olide, 9,11-dehydroergosterol peroxide, Ergosterol peroxide, 3,5,8-trihydroxy-24- methylcholest-6,22-diene, 9,19 cyclolanost-24-en-3-ol-acetate, campesterol, stigmasterol, gamma-sitosterol, desmosterol, stigmasta-5,24(28)-dien-3-ol, Ergost-22-en-3-ol.[61-65]

Flavonoids: Quercetin,[66] Rutin,[67] Quercitrin,[68] 5-hydroxy-3,7-dimethoxyflavone- 4'-*O*-*β*-glucopyranoside,[69] Quercetin-3-*O*-rutinoside,[70] Kaempferol-3-*O*-rutinoside, Isorhamnetin-3-*O*-rutinoside, 5-hydroxy-3,7-dimethoxyflavone-4'-*O*-*β*-glucopyranoside,[71] *O*-methyl resorcinyl-*β*-*D*glucuronopyranosyl (2→1)-*β*-*D*-glucopyranosyl-(2→1)-*β*-*D*-glucopyranoside,[72] 4-methoxy-3-(methoxymethyl) phenol.[73]

Miscellaneous: 2-methoxy-4-vinylphenol, phenol-4-methoxy-3-(methoxy methyl),[74] 8-octadecenoic acid, 1-(2′,5′-dimethoxyphenyl)-glycerol, 12-*O*-benzoyllineolon,[75] 12-*O*-benzoyl deacetylmetaplexigenin, 2,3 dimethoxyphenol,[76] 2,5-dimethoxyphenol, 2-formyl-5-hydroxymethylfuran, Calotropone, Gofruside.[77]

HEPATOPROTECTIVE EXTRACTSOF *CALOTROPIS PROCERA*

Various researchers explored the potential of a range of extracts of different parts of

*Calotropisprocera*plant for the liver protection by using different *in-vitro* and *in-vivo* models.

Flower of ***Calotropis procera***: Setty *et al.,* 2007 evaluated the hydro-ethanolic extract of flower at dose of 200mg/kg and 400mg/kg against the paracetamol (2g/kg) induced hepatotoxicity. Higher dose of paracetamol is oxidized by the *N*-acetyl-*p*-benzoquineimine and causes the elevation of SGPT, SGOT, ALP, bilirubin, cholesterol and decreases the level of GSH and HDL. After the treatment with 200 and 400mg/kg of hydroethanolic extract, the elevated level of SGPT decreased from 281.18±0.65 to 161.28±0.94 & 86.86±0.63U/I, SGOT level from 403.16±1.15 to 285.16±0.56 & 152.35±0.60, ALP level from 436.33±1.33 to 286.43±1.27 & 181.65±1.00, TB level from 3.42±0.11 to 1.45±0.06 & 1.07±0.04 respectively. They concluded that the hepatoprotective potential of flower extract was a result of prevention in depletion of GSH level.[78]

Other study was conducted by Kamil*et al.,* 2014 on the hydro-ethanolic extract of flower of *Calotropisprocera* against the anti-tubercular drugs. The study was conducted at the dose of 150mg/kg, 50mg/kg and 100mg/kg of extract, isoniazid and rifampicin respectively. The level of ALT (41.83±7.09 to 13.83±2.72), AST (189.92±17.3 to 113.5±8.7), ALP (154.67±18.5 to 83.33±11.3) and TB (0.61±0.07 to 0.37±0.03) were reduced after treatment with extract. The histology showed the normal architecture of liver cells.[79]

Root bark of ***Calotropis procera***: Chavda *et al.,* 2010 examined the hepatoprotective potential of methanolic extract of root bark of *Calotropis procera* against the carbon tertachloride (0.8mL/kg) induced hepatotoxicity. The researcher also examined the sub fractions hexane, chloroform and ethyl-acetate for hepatoprotective potential at the dose of 200mg/kg. The result was analyzed by the biochemical parameters and histological parameters. The result of biochemical analysis for methanol, hexane, ethyl-acetate and chloroform showed the reduction of elevated level of SGOT from 309.2±33.1 to 224.9; 203.3±29.7 to 136.5±11.0, 146.2±13.0 and 174.2±21.1; the SGPT level from 684.2±29.2 to 170.8±12.1; 733.4±61.4 to 153.1±20.1, 207.2±37.3 and 682.8±32.6; the ALP level from 48.2±7.6 to 16.3±1.8; 45.0±6.3 to 12.2±0.6, 13.1±2.9 and 38.2±3.3; the TB level from 1.03±0.2 to 0.30±0.06; 0.84±0.088 to 0.20±0.014, 0.195±0.010 and 0.48±0.126 respectively. The histology of CCl_4 intoxicated animals showed the presence of centrilobular necrosis, fatty degeneration, cytoplasmic vacuolization and disturbed hepatocytes while the hexane and ethyl acetate fraction treated animals showed the sign of protection.[80]

Another study conducted by Dahiru*et al.,* 2013 to explore the hepato-nephroprotective potential of ethanolic extract of root bark of *Calotropisprocera* against the CCl_4 induced toxicity in female rats. The study was conducted at the dose of 150 and 300mg/kg of extract and 0.8mL/kg dose of toxicant. The result was analyzed by liver and kidney biochemical parameters. The liver markers were significantly reduced after the treatment with extract. The level of ALT was altered from 30.0±6.7 to 31.8±6.3IU/L and AST level from 130.3±8.7 to 94.7±8.2 IU/L, the level of total bilirubin was also reduced from 2.45±0.03 to 1.91±0.14 at the dose of 300mg/kg. The extract did not show any protective effect on kidney rather it show synergistic action with toxicant and increased the level of creatinine and urea level.[81]

Leaf of ***Calotropis procera***: Agbaje*et al.,* 2016 studied the hepatoprotective potential of aqueous leaf extract of *Calotropisprocera*at the dose of 150, 400 and 800mg/kg against the paracetamol induced hepatotoxicity (150mg/kg). The result was estimated on the basis of biochemical parameters and histopathological examination of liver. The extract lowered theelevated level of liver biochemical markers like AST level reduced to 88.70±26.90 from 118.94± 21.94; ALT level was reduced to 54.76±13.32 from 69.6.±18.10 and ALP level was altered to 177.94±42.90 from 158.83±7.26 at the dose of 800mg/kg along with paracetamol at 150mg/kg.[82] Another study conducted by Ali *et al.,* 2015 on different extracts (ethanol, chloroform and aqueous) of leaves and latex from the *Calotropisprocera* at the dose of 200 mg/kg. Carbon tetrachloride was used as toxicant at dose of 2mL/kg twice a week. Liver biochemical parameters were analyzed to check the potential of extracts and latex. The result showed that extracts and latex significantly decreased the elevated level of AST {275.36±25.65 to 298.34±6.43(A), 175.6±13.34(C), 178.7±2.39(E) and 168.9±4.19(L)}, ALT{229.62±5.56 to 180.34±2.54(A), 159.59±5.67(C), 156.6±2.23(E), 149.5±2.65(L)}, ALP{559.72±25.2 to 350.12±19.3(A), 250.34±14.4(C), 248.35±11.5(E), 225.41±13.9(L)} and TB{1.255±0.29 to 0.982±0.36(A), 0.978±0.15(C), 0.802±0.25(E), 0.765±0.23(L)}.[83]

Further Olaleye*et al.,* 2008 studied the hepatoprotective effect of ethanolic extract of *Calotropisprocera*leaves against the acetaminophen and hepatitis virus induced liver toxicity. Liver toxicity was produced by the oral administration of 2 g/kg of acetaminophen and 2 mL of hepatitis infected serum to the albino rat. Leaves extract was given at the dose of 200 and 400 mg/kg body weight. The extract showed significant dose dependent decrease in serum AST, ALT, ALP and bilirubin level and increased in total protein concentration.[84]

Stem of ***Calotropis procera***: Sharma *et al.,* 2011 explored the hepatoprotective potential of stem ethanolic extract of *Calotropisprocera* against the CCl_4 induced liver toxicity. The study was conducted at dose of 250 & 500mg/kg of stem ethanolic extract and 2mL/kg of toxicant dose. The result was analyzed at the end of seven days by biochemical and histological parameters. The extract reduced the elevated level of SGOT (280.58±29.83 to 173.28±8.02 & 151.2±17.69), SGPT (225.52±17.83 to 103±2.41 & 115.96±16.37), ALP (605.82±31.38 to 216±23.78 & 205±15.094) and TB (1.238±0.20 to 0.792±0.04 & 0.698±0.08) on both the dose of extract. After the treatment with extract the histology showed the normal liver architecture with no necrotic changes and normal central hepatic vein.[85]

HEPATOPROTECTIVE CHEMICAL CONSTITUENTS OF *CALOTROPIS PROCERA*:

Many researchers worked on different extracts of *Calotropis* species having hepatoprotective potential and isolated the chemical moieties that are responsible forhepatoprotective potential. Many biomolecules had been studied, are as follows:

Calotropagenin: Al-Taweel *et al.,* 2017 isolated the calotropagenin from the ethanolic extract of *Calotropisprocera* leaves and evaluated the hepatocytotoxic potential using the HepG2 cell lines. The result was analyzed by cell viability assay method. The IC_{50} for calotropagenin was found to be 10.40±0.98 µg/mL. The result of the study revealed that calotropagenin has significant antiheptocytotoxic potential as compared to ethanol leaf extract (IC_{50} 27.40±1.65 µg/mL).[86]

α-Amyrin: Alpha amyrin is a pentacyclictriterpene widely distributed in the leaves of the *Calotropis procera*. Singh *et al.*, 2015 explored its modulatory potential for hepatic oxidative stress using *wistar albino* rat as experimental animal. The hepatic oxidative stress was induced by intra-peritoneal injection of carbon tetra chloride at 0.2 mL/kg dose. Along with the toxicant animal also received the α-amyrin at dose of 20 mg/kg for 30 days. The result was analyzed by assessment of GGT, AST, ALT, LDH, ALP, GDH, ACP, SDH, GSH, GSH-Px, GST, cytochrome-P-450 and LPO. The result revealed that antioxidant action of α-amyrin was due to blocking of P-450 and inhibitions of ROS.[87]

Lupeol: Lupeol is a triterpene that is widely distributed in nature due to wide variety of pharmacological potential like anti-oxidant, anti-lithiatic and antidiabetic effects.[88,89] It is present in the flowers of *Calotropisprocera*. Prasad *et al.*,2007 evaluated the hepatoprotective potential of lupeol against 7,12-dimethylbenz(a)anthracene (DMBA) induced hepatotoxicity at dose of 50 mg/kg. Lupeol was given at the dose of 25 mg/kg. The oxidative stress induced by DMBA was significantly decreased by lupeol by downregulation of Bcl-2 and upregulation of proapoptoticBax and Caspase 3 activity in animal liver. The result showed that lupeol has hepatoprotective potential by inhibition of apoptosis.[90]

Ursolic acid: Chemically the urosolic acid (3-β-hydroxy-urs-12-ene-28-oic acid) belongs to the class of pentacyclictriterpenoid carboxylic acid. Lots of studies were conducted to evaluate its hepatoprotective potential. It is present in the leaves of *Calotropis procera* as the active constituents.[91] Gabriel A. Guti´errez-Rebolledo *et al.,* 2016 explored the hepatoprotective potential of urosolic acid with the oleanolic acid at the doses of 100 and 200 µg/mouse/day against the anti-tubercular induced liver toxicity in male BALB/c mice. The result of the study revealed that mixture of urosolic acid with oleanolic acid significantly reduced the elevated level of AST and ALT level in treated animals. The result also showed the positive sign in histopathologicalstudies.[92]

Another *in-vitro* study was undertaken by Kishen *et al.,* 2019 to evaluate the hepatoprotective potential of urosolic acid against the CCl_4 (1%) induced toxicity in HepG2 cell lines. The percentage of cell viability was measured by MTT assay.[93] The result of the study revealed that at complete dose (i.e. 100µM) of urosolic acid the percentage cell viability was found to be 85%.

One more study was conducted by Ali *et al.,* 2019 on the isolated urosolic acid for chemo preventive effect of *N*-diethylnitrosamine (200mg/kg) induced hepato-carcinogenesis. HepG2 cell lines were used for the *in-vitro* activity and *wistar albino* rats were used for *in-vivo* study. The *in-vitro* chemo-preventive potential of urosolic acid was evaluated at concentrations of 100, 50, 25, 12.5, 6.25, 3.125, 0.78 and 1.56 Ug/mL by using the MTT assay method. The *in-vivo* potential was evaluated on male *Wistar albino* rats at dose of 500mg/kg. The result of the study revealed that urosolic acid significantly restore the elevated level of serum biochemical parameters and hepatocytes architecture.[94]

Colchicine: Colchicine is lipid soluble tricyclic alkaloids that are used to treat various diseased conditions like rhemumatic, gout, pericarditis and rheumatic arthritis. It is present in the leaves of *Calotropisprocera.*[95] Martinez *et al.,* (1995) studied the protective effect of colchicines against the CCl_4(0.5 mL/100g) induced liver damage and by inhibiting the cytochrome *p*-450 effect. The colchicine was given at the dose of 10 µg/animal/day. Apart from the cytochrome *p*-450 effect, other biochemical investigation like ALT, AST, GGT,

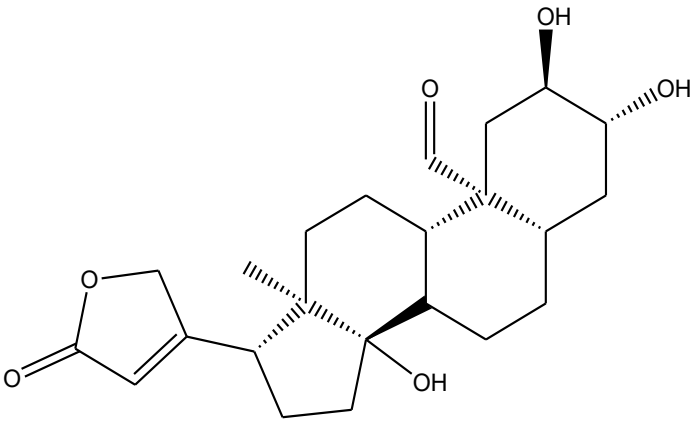

Figure 1 Structure of Calotropagenin

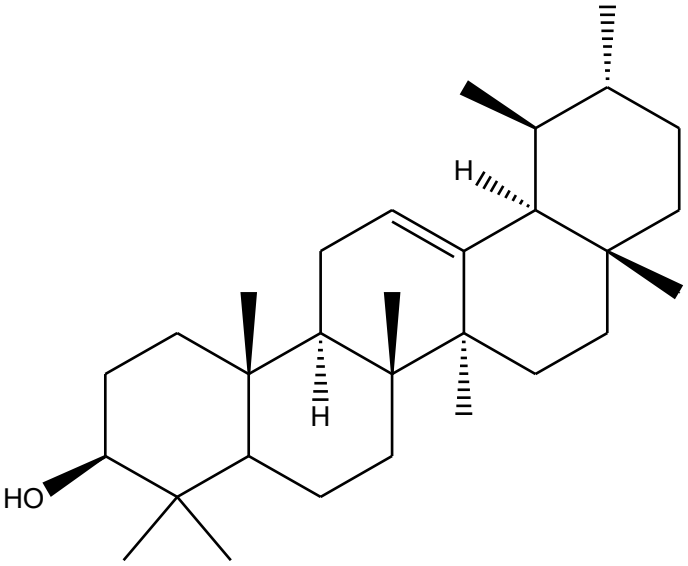

Figure 2 Structure of α-Amyrin

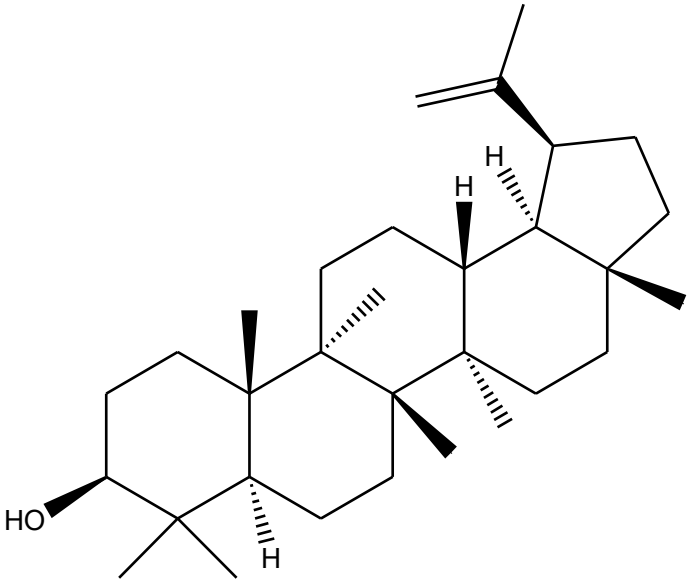

Figure 3 Structure of Lupeol

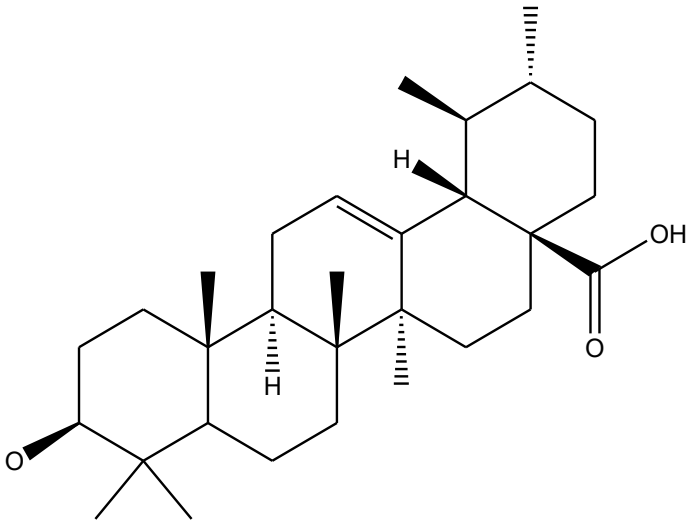

Figure 4 Structure of Urosolic Acid

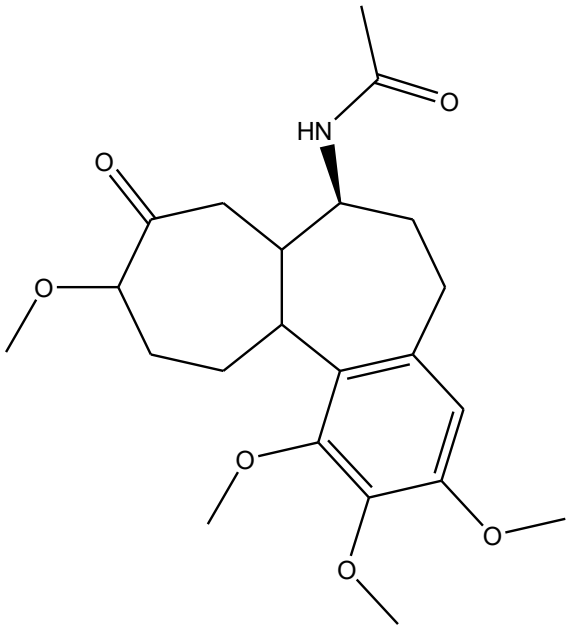

Figure 5 Structure of Colchicine

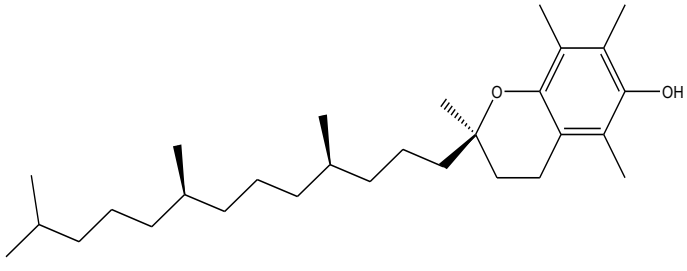

Figure 6 Structure of α-Tocopherol

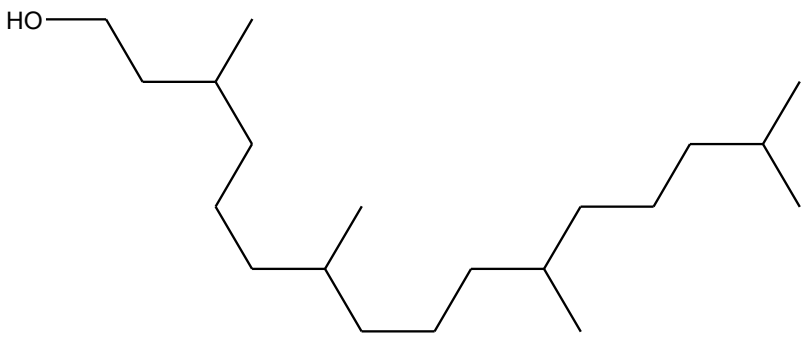

Figure 7 Structure of Phytol

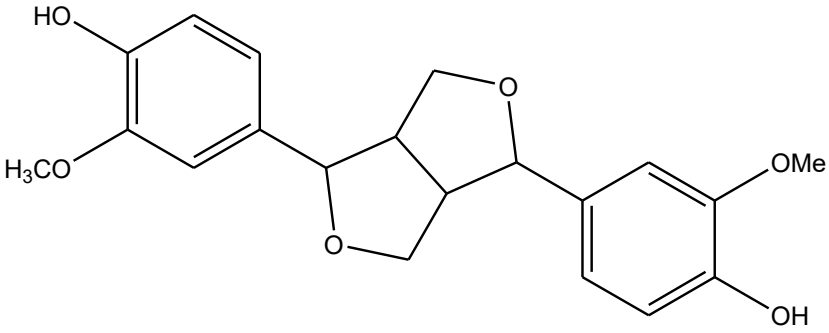

Figure 8 Structure of Pinoresinol

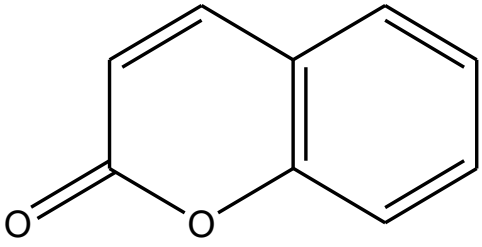

Figure 9 Structure of Coumarin

LPO, MDA and *p*-nitroanisole-*o*-demethylase level were also undertaken to evaluate the protective effect of colchicine. The result of the activity showed that colchicine significantly reduced the cyctochrome*p*-450 level and *p*-nitroanisole-*o*-demethylase activity at the same extent.[96]

α-Tocopherol: α-Tocopherol is a member of fat soluble vitamin that are also synthesized as a lipophillicantioxidant from the green part of all plants. α-Tocopherol is a very good scavenger of lipid peroxy radicals and prevent the cells during oxidation.[97] α-Tocopherol is the active chemical constituents present in the leaves of *Calotropis procera.* Chalouati*et al.,* 2019 studied the protective effect α-tocopherol against hexachlorobenzene (4 & 16 mg/kg) induced liver toxicity. Animals were pretreated with α-tocopherol at dose of 100 mg/kg. Various biochemical (AST, ALT, ALP and LDH), antioxidant (LPO, GSH, SOD and CAT) and histological parameters were analyzed to evaluate the hepatoprotective effect of α-tocopherol. The result of the study revealed that treatment with α-tocopherol significantly reduced the elevated level of biochemical and antioxidant markers that was confirmed by histological study.[98]

Phytol: Phytol is a phytoconstituent that is widely distributed in nature. It is a member of diterpene group of long chain unsaturated acyclic alcohols (3,7,11,15-tetramethylhexadec-2-en-1-ol) present in the leaves of *Calotropis procera*. Gupta *et al.,* 2019 studied the hepatoprotective effect of phytol against the ethanol induced (3.76 g/kg) liver toxicity in *Wistar* rats. Numerous biochemical parameters such as SGPT, SGOT, ALP, TG, TP, SOD, CAT and GSH were studied to evaluate the potential of phytol at a dose of 100 mg/kg and 200 mg/kg. The result of the study showed that phytol significantly reduced the level of SGPT, SGOT, ALP, TG, cholesterol and bilirubin, with this, phytol increased the level of TP, SOD, CAT and GSH.[99]

Pinoresinol: It is a member of lignan family that is generally linked with the two polypropanoid units. Chemically the pinoresinol is a tetrahydro-1*H*, 3*H*-furo[3,4-*c*]furan type of lignin that is found in the leaves of *Calotropisprocera*.[100] Kim *et al.,* 2010 explored thehepatoprotective potential of pinoresinol against the CCl_4 induced liver toxicity in mice model. In this study the pinoresinol at the doses of 25, 50, 100 and 200 mg/kg were injected before the CCl_4 at dose of 20 µL/kg injections. The result of the study revealed that pinoresinol significantly treats the acute liver injury from the oxidative stress and inhibition of inflammatory mediators via NF-*k*B and AP-1.[101]

Coumarin: It is a very broad group of naturally occurring phytochemical that are 1,2-benzopyrone. It is present in *Calotropis procera* leaves as a hydrocoumarin. Atmaca *et al.,* 2011 studied the hepatoprotective potential of coumarin and its derivates on the CCl_4(1.25 mL/kg) induced liver toxicity in rats. The protective effect of liver was analyzed on the basis of anti-oxidant markers such as MDA, SOD, CAT as well as GGT and LDH level. The result of the study revealed that coumarin structure (30 mg/kg) plays a significant role in reducing the oxidative stress induced liver toxicity.[102]

FUTURE PROSPECTIVE

The plants and plant inferred phytomolecules are the source for never-ending wellspring in upcoming years. *Calotropis procera* is the spice with brimming with circumstances and supports the analysts for investigation of dynamic lead molecule for hepatoprotectivedrugdesign. Different molecules

were separated from the *Calotropis procera* and assessed for their hepatoprotective potential and the outcome urges the researchers to accomplish more exploration on these molecules. For future work more examinations are needed for distinguishing proof of careful system behind these molecules as hepatoprotective agents. This review will help to design pharmaceutical products having hepatoprotective potential based on the scientific validation of the folk-claims of *Calotropis procera* plant.

CONCLUSION

Calotropis procera(Ait) R. Br. is an erectile shrub with full of medicinal values. Various pharmacological activities were conducted to explore the potential of plant parts. There is an urgent need to combat the hepatic epidemic in the region and other developing countries facing health as well as an economic burden. Hence, realizing the enormous potential of this plant the literature review is articulated.

Herbal system of medicine is continuously growing field of research for the different reasons like increasing adverse effects, misbranding and adulteration of allopathic medicine. Medicinal plants like *Calotropis procera* is the ocean of various pharmacological activities. This review is mainly focused on the hepatoprotective potential of the different parts of *Calotropis procera*. Scientist explored the potential of extracts and some isolated molecule of *Calotropis procera*as the protection of liver from various chemical stimuli. There is need to validate the *Calotropis procera* scientifically for hepatoprotective.

LIST OF ABBREVIATIONS

CCl_4	-	Carbon tetrachloride,
LPO	-	Lipid peroxidation,
TP	-	total protein,
ALT	-	Alanine Transaminase,
SGPT	-	Serum Glutamic Pyurate Transaminase,
AST	-	Aspartate Transaminase,
SGOT	-	Serum Glutamic oxaloacetic transaminase,
ALP	-	Alkanine phosphatase,
CAT	-	Catalase,
SOD	-	Superoxide dismutase,
GSH-Px	-	Glutathione peroxide,
TB	-	Total Bilirubin,
DB	-	Direct Bilirubin,
GSH	-	Glutathione,
ALB	-	Albumin,
GSH-Rd	-	Glutathione reductase,
MDA	-	Malondialdehyde,
GGT	-	Glutamyltranspeptidase,
LDH	-	Lactate dehydrogenase,
p.o.	-	per oral,
i.p.-		intraperitoneal,
s.c.	-	subcutaneous

CONSENT FOR PUBLICATION

I Yogesh Murti as a corresponding author on behalf of all the co-authors gives my consent for the publication of this manuscript for Discovery Phytomedicine as a review article.

CONFLICT OF INTEREST

The authors declare that they have no conflicts of interest concerning this article.

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AUTHORS' CONTRIBUTIONS

Krishn Kumar Agrawal conceived of and wrote the manuscript. Yogesh Murti designed and edited the paper. Both authors read and approved the final manuscript.

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