REVIEW
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Multiple pharmacological properties and uses of an edible herb - *Cassia tora*

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Conflict of Interest

The authors declare that they have no conflict of interest.

Abbreviations

TCM: Traditional Chinese Medicine; MoA: Mode of Action; IgE: Immunoglobulin E; CTE: Cassia tora extracts; PCA: passive cutaneous anaphylaxis; EBV-EA: Epstein-Barr Virus Early Antigen; MeOH: methanolic; HeLa: human cervical cancer cells; COX2: Cyclooxygenase 2; iNOS: Nitric Oxide Synthase; MMPs: Matrix metallopeptidases; MTT: Methyl Thiazolyl Tetrazolium ; Bap: Benzo-a-Pyrene; TrP1: Tryptophan biosynthesis protein; LPL: Lipoprotein lipase.

Citation

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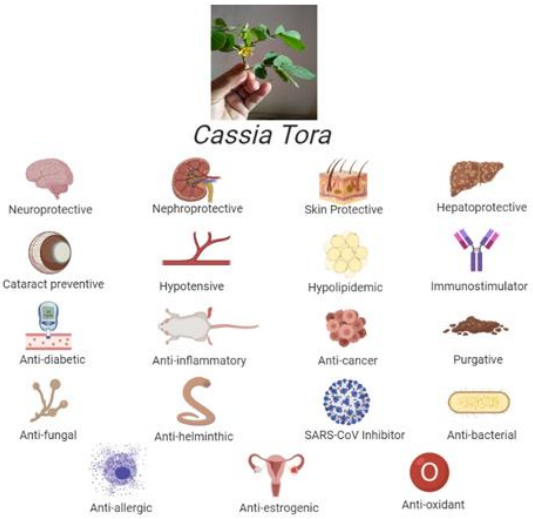
Abstract

Cassia tora Linn. More commonly known as 'Charota' in hindi language in India, is a rainwater wasteland herb. For years, the leaves and seeds of *Cassia tora* have been used in the Ayurveda, Traditional Chinese Medicine (TCM), and folk medicine of tropics for the various medicinal properties it possesses. By reviewing various literature on the plant, it was found that it is great for health as it possesses several protective properties like: hepatoprotective, nephroprotective, cataract protective, skin protective, and neuroprotective properties. Apart from these properties like, vasodilatory, anti-tumor, anti-oxidant, laxative, anti-diabetic, anti-inflammatory, anti-estrogenic, are also significant medicinal activities that can be further used to develop neutraceuticals for diseases like cancer and diabetes. Lastly, the compounds found in Cassia Tora are also efficient anti-bacterial, anti-fungal and anti-helminthic agents. Some of its medicinal properties have been reported only in ethnomedicine, while some tested in model systems, and some verified through clinical trials. We evaluate the current state of literature on these medicinal activities. We have found this leguminous herb to have potentially multiple characteristics that might help in mitigating current pandemic with literature evidence of anti SARS-CoV activity. Further, an *in-silico* analysis of the molecule Aurantio-Obtusin (AO) showed efficient binding to various SARS-CoV2 proteases and host factor molecules involved in inflammatory pathways. However, more experimental and clinical studies with single isolated and purified natural compounds are warranted to confirm such useful activities of the wasteland herb, for it's health food, medical and economic utilization.

Keywords: Cassia; *Cassia tora Linn*



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Highlights

- Activity across major health indications including current pandemic situation.
- Easy growing across the world.
- Natural pharmacophores amenable to further development.
- Nutraceutical source of health and well being.
- Single herb plant with poly-pharmacological potential including anti-SARS activity.
- Molecule Aurantio-Obtusin shows significant Anti-inflammatory and anti-SARS activity.

Introduction

Cassia tora, also known as Senna Tora, Foetid Cassia, Sickle Senna, Wild Senna in English, and Charota, Chakvad, Chakavat in Hindi, and Chakramard in Sanskrit, is an herb that grows in wastelands.

The use of Cassia Tora as a healing herb stems from Ayurveda. Rural as well as tribal people of Madhya Pradesh, India, have been using the leaves and the seeds of this plant for different kinds of aliments. Further, Traditional Chinese Medicine (TCM), has plenty of proof and experience regarding the application of cassia seeds (also known as Jue Ming Zi) and leaves in drug preparation as well as using them to cure various diseases. The weed form of the crop has been analyzed since ancient times and as per Ayurvedic records, it was known to contain acrid, laxative, anthelmintic, ophthalmic, cardiotonic and expectorant properties. Since ancient times in China, the seeds of Cassia have been used as aperients, antiasthnic and diuretic agents [1].

It is a semi-wild annual herb grown widely in different places of south-east Asia including India, Northern Australia and Americas [2]. As per botanical classification systems, it belongs to the Family-Leguminosae. It is an annual foul-smelling (fetid) herb that can grow up to 30-90 centimeters in length. The plant is a hermaphrodite, meaning it grows both the male and female flower parts. The leaves of *Cassia tora* which are roasted in oil and eaten in parts of India; are paripinnate, can grow up to 10 centimeters in length, and have an obovate structure. The flowers are corymbose raceme. They are pentamerous (having 5 petals) and also have 5 sepals. They are yellow in color [3]. The flowering period is post-monsoon in India (August-September). The seeds of *Cassia tora* are known to possess great medicinal value. These are too, roasted and consumed. The seeds are about 1 centimeter long and 3-4 millimeters thick. They are oblong and brownish-black in color. They have a bitter taste. Early chemical constituent studies were carried out on two species of plants in genus- *Cassia*, viz Cassia tora and Cassia obtusifolia; and were found to be distinctly of different profiles [4].

Since the plant has such immense use in tackling various local and fatal diseases, backed up by ancient as well as modern literature; the aim of this review is to provide an updated information as well as to highlight the Mode of Action (MoA) of the bioactive compounds in the plant as present in established literature.

The pharmacological properties reported for the herb Cassia tora

Systems or Molecule Regulatory Properties

Anti-Allergic properties. *Cassia tora* contains a bioactive molecule, Aurantio-Obtusin; which is responsible for the Anti-allergic properties. This biomolecule inhibits the production of mRNA related to immune modulator cytokines. Further, it suppresses Immunoglobulin E (IgE) mediated Fc ε RI signaling, through phosphorylation of various protein kinases (Syk, Protein Kinase Cμ, Phospholipase Cγ, etc.). It also blocks mast cell-dependent PCA. However, Aurantio-Obtusin has shown antiplatelet activity in rats. The effects of *Cassia tora* extracts (CTE) and its active compound Aurantio-Obtusin on IgE-sensitized allergic reactions was studied in mast cells and passive cutaneous anaphylaxis (PCA models). The study demonstrated that CTE and aurantio-obtusin suppressed degranulation, histamine production, and reactive oxygen species generation while inhibiting the mRNA expression of tumor necrosis factor-α and interleukin-4 [5].

Anti-Cancer and Anti-Metastatic properties. Emodin present in *Cassia tora* also displays substantial *anti-tumor activity*. This molecule inhibits angiogenic and metastasis regulatory processes within cells. However, this extract can also hamper with the electron transfer process in long-term and hence be cytotoxic [6]. There are cases when cancer patients display levels of Epstein-Barr Virus Early Antigen (EBV-EA) in the body. Inhibition of its activity has been displayed by *Cassia tora* in Raji Cells [7].

Further, the methanolic (MeOH) extract of *Cassia tora* shows anti-proliferative action. The antiproliferative activity of CTME was studied along awith Cisplatin, an anticancer drug using human cervical cancer cells (HeLa). Proliferation of cells was measured by MTT assay, cell DNA content by modified diphenylamine method and induction of apoptosis by Caspase 3 activity. The CTME extract induced a marked concentration dependent inhibition on proliferation, reduced DNA content and apoptosis in HeLa cells [8, 9].

Cassia tora shows anti-cancer and anti-metastatic activity in Human tongue carcinoma TCA8113 cells. In a study, the methanolic extract of *Cassia tora* was able to regulate the activity of Bcl and Bax by controlling mRNA expression. It also displayed the apoptosis of cancer cells. Further, the plant extracts are also known to down-regulate the expression of the inflammatory conditions associated Cyclooxygenase 2 (COX2) gene that plays an important role in colon cancer. It is also known to down-regulate the expression of inducible Nitric Oxide Synthase (iNOS) which acts as a target for colon cancer prevention [9–11]. In colon 26-M3.1 cells, the anti-metastatic effect observed was due to the inhibition of the synthesis and activity of Matrix metallopeptidases (MMPs) [1].

In another study carried out to identify constituent(s) with potential cytotoxic effect on cancer cells, IC_{50} values of ethanolic leaf extract of Cassia tora using two different human cancer cell lines- namely HeLa and HSC–1; was determined using Trypan blue exclusion methods and Methyl Thiazolyl Tetrazolium (MTT) assays. The active compound isolated was reported to be Friedelin [12].

Anti-Diabetic. The butanol fraction of *Cassia tora* has been shown to lower post-prandial blood glucose levels. This was achieved by increasing insulin production. This is achieved by pancreatic stimulation [13]. In a recent study conducted by Indian scientists, ethanolic extract of *Cassia tora* seed extracts and standard drug-glibenclamide; prepared in aqueous gum acacia (2 %, w/v) suspension was fed orally to streptozotocin induced male adult diabetic rats of Charles Foster strain, as a model of Diabetes for 15 days. Biochemical parameters measured in normal, diabetic control, standard treatment (600 μg/kg) and Cassia extract treated (500 mg/kg) animal groups were further compared. The authors report significant antidiabetic, anti-dyslipidemic and antioxidant potential of *Cassia tora* seeds in prevention of diabetic dyslipidemia and related complications [14]. The n-butanol soluble; ethanolic extract preparations of Cassia tora seeds particularly column chromatography based separated fraction 6 studied in alloxan treated diabetic rat models show decreased elevated blood glucose levels and markers of hepatic and renal dysfunctions in the diabetic rats [15].

Further, AGE products have been known to worsen the complications of diseases like diabetes. Thus, molecules like emodin and obtusifolin found in *Cassia tora* are well known for inhibiting the formation of these end products. The molecules emodin and obtusifolin display a dose-dependent reduction of AGE-BSAs. They inhibit CML-BSA, which is well known for diabetic pathogenesis [16].

Anti-Estrogenic. *Cassia tora* possesses estrogenic/anti-estrogenic activity due to the presence of biomolecules like dihydroxynaphthalenes, rubrofusarin, nor-rubrofusarin, nor-toralactone, hydroxymusizin, torachrysone. These compounds show a concentration-dependent Inhibition of 17-Beta-Estradiol and inhibit Breast cancer MCF-7 cell proliferation [17]. There are documented evidences of the Cassia tora leaves being used by tribal communities of Rajasthan for similar effects and as source of non-oxalate containing nutrients [18].

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Anti-Genotoxic. The bioactive molecules like chrysophanol, emodin, and rhein also display anti-genotoxic activity. The inhibitory activity against Benzo-a-Pyrene (BaP) induced DNA damage has been demonstrated in HepG2 cells. These molecules suppress the mutagenicity of the Tryptophan biosynthesis protein (TrP1) gene by neutralizing its reactive intermediate. However, the side effects that can be attributed to Emodin and Rhein are that these molecules can cause skin, eye, and respiratory tract irritation in long term [19, 20].

Anti-Inflammatory and Anti-Rheumatic. The biomolecule responsible for the anti-inflammatory property of *Cassia tora* is anthraquinone glycoside. This molecule has shown reduced edema and swelling in rats through the inhibition of Dextran, Histamine (5-HT), and serotonin activity. However, this molecule is also known for causing diarrhea in mice and acts as a laxative [21]. The anti-inflammatory effect of aurantio-obtusin isolated from dried seed extracts of Cassia tora has been studied on lipopolysaccharide-(LPS)-induced RAW264.7 cells in vitro and elucidation of the possible underlying molecular mechanisms evaluated. The pro-inflammatory enzymes and cytokines expression levels were measured using RT-PCR. Aurantio-obtusin was found to significantly decrease the mRNA levels of NO, PGE2, and also inhibited the protein expression of COX-2, TNF-α and IL-6 at protein expression levels again at p values of 0.01 thus affecting the downstream activity of transcription factor involved in Inflammatory processes-NFkB [22].

Pro-inflammatory cytokines viz., IL-1α, IL-1β, IL-6, IL-8, IL-17 and TNF-α contributes to the pathogenesis of chronic inflammatory skin diseases such as psoriasis and has been a target for the development of the new anti-psoriatic drug. In a cell line-based study, isolated flavonoids from Cassia tora were tested for the effect of isolated compounds using HaCaT cells, in a rapidly multiplying human keratinocyte cell line as a model of epidermal hyper proliferation seen in Psoriasis. Among the isolated compounds, several compounds including Luteolin-7-O-β-glucopyranoside showed significant antiproliferative activity in HaCaT cells. The results showed that the selected plants and isolated flavonoid-Formononetin-7-O-β-D-Glucoside have potential effects as anti-inflammatory agents by inhibiting the release of pro-inflammatory cytokines supporting the folkloric utilization [23].

Another Korean study recently investigated anti-inflammatory effect of aurantio-obtusin isolated from *Cassia tora* as 50% ethanol extracts; on the lipopolysaccharide (LPS)-stimulated inflammatory response in murine macrophage cell line (Raw 264.7) much similar to Chinese study. The study of its effect on Prostaglandin synthesis pathway mediated by PGE2 levels were found to be decreased in a dose-dependent manner by Aurantio-obtusin. The release of interleukin-1β (IL-1β) and IL-6 was found to be reduced as well. Specifically, Aurantio-obtusin was reported to suppress LPS-induced I κ B-α degradation [24].

Anti-Lipogenic. The effect of Cassia tora extract and chrysophanol, which is widely used as anti-inflammatory agent on the heat shock effect in sebocytes was examined in a study for querying its effect on lipogenesis. Chrysophanol found in *Cassia tora* is known to be anti-lipogenic in nature. It suppresses the upregulation of PPARγ, FAS, and IL-1β, thus influencing skin sebum production [25].

Anti-Mutagenic. The anti-mutagenic activity of *Cassia tora* can be attributed to various compounds found in it. From the n-Butanol (n-BuOH) extract containing cassiaside, rubrofusarin, gentiobioside can be obtained while from the Dichloromethane (CH_2-Cl_2) extract; chrysophanol, chryso-obtusin and aurantio-obtusin is isolated. These biomolecules are known to accomplish the anti-mutagenic activity by inhibiting the indirect mutagen Aflatoxin B1 (AFB1) as demonstrated using AMES test on S. typhimurium or by scavenging the electrophilic intermediates which are responsible for inducing mutations [26–27].

Anti-Nociceptive and Spasmogenic. The Methanolic Extract (MeOH) of *Cassia tora* has shown antinociceptive and spasmogenic activity. This extract showed a concentration-dependent contraction of ileum and jejunum smooth muscles in Guinea pig and rabbit respectively. In mice, it increases intestinal transit [28].

Anti-Oxidant. In a Chinese study, methanolic extracts from C. tora L. (MECT) showed stronger antioxidant activity and gave higher yields of extract than other organic solvents. The MECT showed stronger antioxidant activity on peroxidation of linoleic acid. MECT at 200 ppm was stronger than 200 ppm of α-tocopherol, but weaker than 200 ppm of butylated hydroxy anisole [29]. The molecules chrysophanol, emodin, and rhein found in *Cassia tora* protect cells because they act as antioxidants. They scavenge the cells for oxygen-free radicals that might have been generated when a mutagen was activated and destroy it [10].

In a controlled rat study, early treatment with *Cassia tora* leaf extracts was shown to protect from isoproterenol (ISO) induced myocardial injury, that included propranolol as standard drug given orally or sub-cutaneous route. Cassia tora extracts, on the other hand given at 200 mg/kg showed significant decrease in level of serum marker enzymes aspartate transaminase (AST), lactate dehydrogenase (LDH), alanine transaminase (ALT), alkaline phosphatase (ALP), changes in the oxidative stress markers like lipid peroxidase (LPO), glutathione (GSH), catalase (CAT), and superoxide dismutase (SOD) that is caused by ISO at 5.25 and 8.5 mg/Kg [30].

Anti-Psoriatic Activity. Another study suggested that the molecules luteolin, quercetin, and formononetin found in *Cassia tora* decreased thickness in the epidermal layer in Healthy male Wistar rats and Swiss albino mice. They further show that these effects are due to inhibition of pro-inflammatory cytokines IL-6, IL-8 and TNF-alpha [24].

Hypolipidemic. The ethanolic extract of *Cassia tora* is known for its hypolipidemic activity. This molecule decreases Low Density Lipoproteins possibly due to the inhibition of cholesterol biosynthesis and an increase in fecal bile acid production. Further, it displays increased High-Density Lipoprotein-cholesterol level which can be due to its inhibitory action on hepatic Triglyceride-lipase enzyme whose role is to otherwise to decrease HDL. The ethanolic extract also decreases serum Triglyceride through catabolism of triglycerides and inhibition of fatty acetyl-CoA and glycerophosphate acetyltransferase activity [31].

Another study found that the seeds of *Cassia tora* when fed to mice activated Post-Heparin lipolytic Activity and Lipoprotein lipase (LPL) activity which is important for lipid catabolism. It also increased bile acid in fecal excretion [32].

Hypotensive or Vasodilatory Effects. The hypotensive property of *Cassia tora* can be attributed to the presence of bioactive molecules like anthraquinone and naphthopyran glycosides. The *Cassia tora* seed extract is responsible for the changes in the basic cardiovascular reflexes and the reduction of vasomotor tone, thus relaxing the blood vessels. They also reported involvement of medullary reticular formation in hypotensive principle of extracts of seeds [33].

Angiotensin-Converting Enzyme is an enzyme that controls vasomotor function. Thus, inhibiting this results in Vasodilation. Anthraquinone glycosides found in *Cassia tora* is well known for inhibiting the activity of ACE [27]. It is also known to act as a receptor for SARS Corona virus Spike protein and aid in invasion of target cells as depicted earlier [25].

Vasodilation is the activity by which blood vessels dilate and the blood pressure is reduced. Such properties are displayed by *Cassia tora* due to the presence of molecules like toralactone-9-O-gentiobioside, physcion-8-O-gentiobioside, glucoaurantio-obtusin. These molecules reduce blood pressure by inhibiting soluble Epoxide Hydrolases (sEH) [34].

Immunomodulation potential. *Cassia tora* acts as a modulator of immune response due to the activity of biomolecules like Rhein, Chrysophanol, Aloe-emodin and Emodin. These molecules display a concentration-dependent increase in the proliferation of PBMC. Ethanol acetate extracts containing anthraquinones of Cassia tora are known to modulate immune responses by stimulating mouse splenocytes at concentration of 10 microgram per ml, while inhibiting production of nitric oxide [35]. Three immunostimulant anthraquinones were identified, viz chrysophanol, isochrysophanol and Aloe-emodin. A concentration-dependent increase in the secretion of interferon-gamma (IFN-γ) and interleukin 10 (IL-10) and an increase in the number of CD4+ T cells have also been displayed.

However, these molecules can be cytotoxic at certain concentrations [36].

Laxative or Purgative effect. The purgative property of *Cassia tora* can be attributed to molecules like aloe-emodin, 1.8-dihydroxy 3-(hydroxymethyl)-anthraquinone. These molecules cause severe purgation and diarrhea and have shown to produce wet fecal matter in mice [37].

Anti-Microbial Properties

Anti-Bacterial. Many early studies have reported anti-bacterial properties of plant *Cassia tora* (Grand 1989). It displays anti-bacterial action due to the presence of molecules like unglycosylated naphthalenes, torachrysone, anthraquinone, traction, aloe-emodin, rhein, and emodin. These molecules show an antibacterial effect against four strains of Methicillin-Resistant *Staphylococcus aureus* (MRSA) and one methicillin-sensitive strain of *Staphylococcus aureus* [38].

Against the strains of *Staphylococcus aureus* and *Lactobacillus,* the ethanolic extract of *Cassia tora* showed the maximum activity when tested using the paper disc method. It also displayed moderate activity against the strains of *Pseudomonas aeruginosa, P.vulgaris,* and *Enterobacter* [39].

Anti-Fungal. When we obtain the seeds of *Cassia tora* and extract its components, we get the compound chrysophanic acid-9-anthrone. This is the compound responsible for its anti-fungal properties against fungal strains like *Trichophyton rubrum, T. mentagrophytes, Microsporum canis, M. gypseum, and Geotrichum candidum*. This anti-fungal action is facilitated by the presence of 100 mg/ml L-ascorbic acid, which acts as an antioxidant [40].

Another study found that 1g/L chloroform ($CHCl_3$) extract of *Cassia tora* (containing molecules like emodin, physcion, rhein, and aloe-emodin) acts as a fungicide for the species: *B. cinerea, E. graminis*, *P. infestans*, and *R. solani*. Out of these molecules, aloe-emodin acts only against *B. cinerea* and *R. solani* [41].

Another study found that the activity of the dealcoholized extract of *Cassia tora* against the fungi *C. albans*, *S. cerevisiae*, and *T. mentagophytes* was studied using the turbidity and spore germination method, and *Cassia tora* leaf extracts displayed fungicidal activity [42].

Anti-Viral (including SARS-Coronavirus) Inhibition. Emodin found in *Cassia tora* leaves shows inhibition of the interaction between the SARS-CoV spike - S protein and the ACE2 receptor complex, which acts as an important entry mechanism for the virus into the human host cell that created an epidemic in 2003 [25]. Other anti-viral activities of methanolic extracts of *Cassia tora* roots have been shown against Newcastle Diseases virus and Vaccinia viruses [43]. In a review of literature for screening of natural products with antiviral activities against different types of the human coronavirus, studies included Cassia tora L., has shown a potential effect against SARS-CoV [44].

Anti-Helminthic properties. The anti-helminthic properties possessed by *Cassia tora* are due to molecules like flavonoids and polyphenolic compounds. Such compounds increase chloride ion conductance in muscle membranes of worms, producing hyperpolarization and reduced excitability, which leads to flaccid paralysis and death of the worm [46]. In a more recent controlled study, ethanol acetate, acetone, methanol and aqueous extracts of Cassia tora seed and seed cover were investigated for their phytochemicals, followed by anti-helminthic activity against Eisenia foetida. Significant activity at highest concentration of 5mg/mL in a dose dependent manner was reported in case of seed extracts when compared to seed cover and was attributed to Emodin and Quercetin [46].

Larvicidal properties. The molecule Ononitol monohydrate found in *Cassia tora* extends the larvae-pupil duration and also shows larvicidal and pupicidal activities on the species *Helicoverpa armigera* and *Spodoptera litura* [47].

Organ Protective Properties

Cataract protection. Effect on eye rejuvenation; specifically, by preventing selenite-induced cataract in rat pups was studied to identify the active components of Cassia tora leaves that produce the effect. The bioactive molecules such kaemferol, chrysophanol, and emodin displayed a reduced production of peroxidase and calpains in lens tissue and also protected the ubiquitin-proteasome pathway in Sprague Dawley Rats. Daily consumption of *Cassia tora* leaves as vegetable is recommended [48].

The biomolecules obtained from *Cassia tora* like emodin, aurantio-obtusin, and chryso-obtusin-2-O-b-D-glucoside showed the inhibition of Rat Lens Aldose Reductase (RLAR) enzyme, which is responsible for cataract in rats [49].

Hepatoprotective. Hepatoprotective effects of Cassia tora against carbon tetra chloride induced liver damage has been studied in albino rats. The efficacy of the treatment was estimated by the serum level marker enzymes: serum glutamate oxaloacetic transaminase, serum glutamate pyruvate transaminase and lactate dehydrogenase. The results of this study reveal the remarkable increase of marker enzymes in induced rats and decreased level in Cassia tora treated ones [50]. The biomolecule Ononitol monohydrate found in *Cassia tora* displays *in vivo* hepatoprotective activity in male rats by decreasing the amount of serum transaminase and inhibiting lipid peroxidation and the tumor necrosis factor- TNFα. It also increases antioxidants and hepatic glutathione enzyme activities [51]. In another recent study, the defatted alcoholic extracts of seeds of *Cassia tora* were screened for hepatoprotective activity using adult Wister albino rats (120-170 g) as the experimental animals, and effects were found to be comparable to Silymarin used as standard hepatoprotective agent [52].

Nephroprotective. Several studies have shown that biomolecules like rubrofusarin-6-O-d gentiobioside, toralactone-9-O-d-gentiobioside, and cassiaside present in *Cassia tora* possesses renoprotective activities. These activities include reduction of proteinuria and decreased expression of AGE and RAGE molecules, in turn reducing glomerular inflammation [49].

The extracts of Cassia Seeds (termed Cassia Semen) are also known for decreasing Collagen-IV and TGF-beta1 expression and for decreasing TGF-beta1 expression by blocking the phosphorylation of ERK1/2 and p38 MAPK in mouse glomerular mesangial cells. Further, these molecules inhibit the activity of NF-kappa-beta (kB) and Smad2 in a dose-dependent manner [53].

Another study found that the molecules obtusifolin, aurantio-obtusin, obtusin, physcion, and chrysophanol found in *Cassia tora* protect the kidneys from ischemic/reperfusion damage. They also reduce the levels of serum creatinine, and Blood Urea Nitrogen (BUN) , and Nitric Oxide levels. Moreover, they were found to reduce the activity of antioxidant enzymes like CAT, SOD, and GPX [54].

Neuroprotective activity. Cassia Tora displays Anti-amyloidogenic properties. Amyloids are aggregates of proteins that are known to be linked to diseases such as Alzheimer's. *Cassia tora* has Polyphenols like Protocatecheuic acid, Catechin, Chlorogenic acid, Caffeic Acid, Vanillin, p-Coumaric acid, p-Coumaric acid, Rutin Hydrate, Quercetin, Kaempferol which have shown anti-amyloidogenic action. This is achieved by the inhibition of the aggregation of AB from monomers and oligomers. It also dis-aggregates pre-existing fibrils [55] It has also been demonstrated for the first time that *Cassia tora* fraction prevents Aβ 1-42 aggregation, inhibits acetylcholinesterase and alleviates Aβ 1-42 -induced oxidative stress in human neuroblastoma cells by the same group [55].

Another study found that the ethyl acetate (CtEA) or methanolic (CtME) extracts of *Cassia tora* reduced paraquat induced reactive oxygen species production, DNA damage, apoptosis, and lipid peroxidation in SK-N-SH neuroblastoma cells [56].

The molecules alaternin and nor-rubrofusarin glucose identified from *Cassia tora* also display neuroprotective activity. Research suggests that Alaternin shows dose-dependent inhibition of peroxy nitrite ($ONOO^-$) mediated nitration, whereas, Nor-rubrofusarin shows a decrease in $ONOO^-$ mediated nitration of tyrosine [57].

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Skin protective. Emodin, which is found in *Cassia tora* is known for it's anti-pigmentation nature. In a study, it was found that under 10mm, emodin is non-toxic and it inhibits the phosphorylation of Kit ligand.

Further, it also blocks the activity of various receptors like epithelial growth factor receptor (EGFR), vascular endothelial growth factor receptor 2 (VEGFR-2), fibroblast growth factor receptor 1 (FGFR-1), and platelet-derived growth factor receptor b (PDGFR-b). This study was conducted on human primary Melanocytes [58].

Bioinformatics evaluation of an anti-oxidant, anti-inflammatory compound from Cassia tora

***In Silico* Analysis of a nutraceutical component – Aurantio-Obtusin**

Aurantio-obtusin is a trihydroxyanthraquinone that is 1,3,7-trihydroxy-9,10-anthraquinone which is by methoxy groups at positions 2 and 8, and by a methyl group at position 6.

IUPAC:

1,3,7-trihydroxy-2,8-dimethoxy-6-methylanthracene-9,10-dione

Molecular Formula: $C_{17}H_{14}O_7$

Molecular Weight: 330.29

Docking of Aurantio-Obtusin with various SARS-COV Receptors and Proteins

A. SARS-CoV-2 CL3_Main Protease (PDB ID: 6Y84)

Organism: Severe Acute Respiratory Syndrome Corona Virus 2 (SARS-COV-2)

The SARS-CoV2 main protease is also referred to as the Mpro, the 3CLpro, and the nsp5 protein in various literature sources. These viral proteins are exclusively being targeted for drug development because these proteases are different from human proteases and actively take part in the replication of the virus [59]. Docking and interaction analysis is presented in Figure 1 ab. Full Fitness Value: -969.20 kcal/mol Estimated oG : -6.49 kcal/mol

B. SARS-CoV-2 Spike (S) protein receptor-binding domain bound with ACE2 (PDB ID: 6M0J)

Organism(s): Severe acute respiratory syndrome coronavirus 2 bound to human receptor complex

The amino acid residues responsible for binding of the SARS-CoV virus with the Angiotensin Converting Enzyme 2 receptor have been observed to be conserved and are present in the SARS-CoV-2 virus [60]. Thus, the ACE2 receptor acts as a cell entry point for the virus. This has been tested using immune-blots.(Hirano and Murakami 2020). Then results are depicted in Figure 2 ab Full Fitness Value: -2125.39 kcal/mol Estimated oG: -7.60 kcal/mol

C. SARS-COV-2 ADP ribose phosphatase (NSP3, PBD ID: 6VXS) Organism: Severe acute respiratory syndrome corona virus 2

The SARS-COV-2 ADP ribose phosphatase, among the 15 non-structural protiens encodes an enormous multidomain Nsp3 , also known as PLpro domain protease. This viral protein interferes with the host innate immune response by removing ADP ribose from RNA [61]. The results are depicted as below, while best docking poses as analyzed are provided in Figure 3 ab . Full fitness value: -1512.16 kcal/mol Estimated ΔG: -7.04 kcal/mole

Docking of Aurantio Obtusin with Inflammatory Proteins

D. NFkappaBeta (NFkB) P50/P65 HETERODIMER COMPLEXED TO THE IMMUNOGLOBULIN KB DNA (PDB ID: 1vkx)

Organism: Mus musculus (structure highly conserved with human)

NFkB or Nuclear Factor kappa-light-chain-enhancer of activated B cells is a protein complex known to be involved in the inflammation pathway and leads to the release and activation of cytokines and interleukins. Full Fitness Value: -3759.18 kcal/mol Estimated oG: -7.43 kcal/mol (Figure 4 ab)

E. Interleukin Receptor 6 (PDB: 1I1R)

It is the interleukin involved in the inflammation of lung tissue during various diseases and is directly inhibited by Aurantio-Obtusin

Full fitness value: -2229.46 kcal/mol Estimated ΔG: -6.96 kcal/mol (Figure 5 ab)

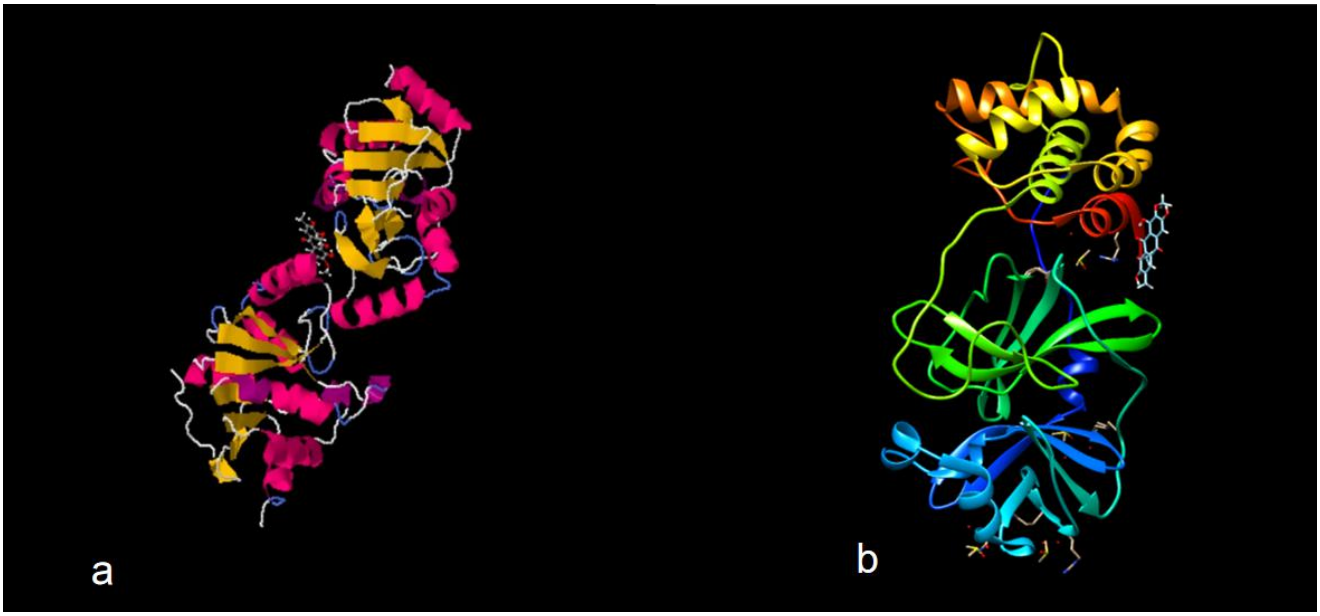

Figure 1 a. Aurantio-Obtusin docked with SARS-COV2 CL3 Mpro (PDB ID: 6Y84) using SwissDock Server based computational tools. b. Aurantio-Obtusin docked with SARS-COV2 CL3 Mpro (PDB ID :6y84) viewed using UCSF Chimera, best pose.

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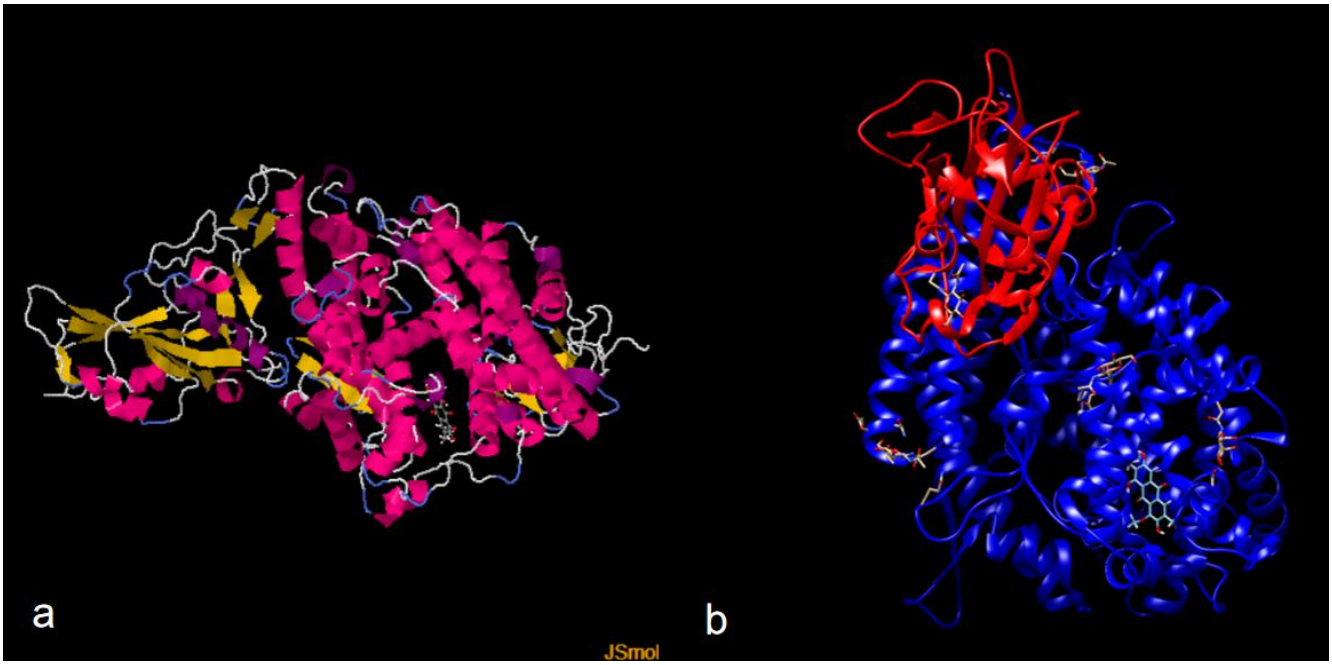

Figure 2 a. Aurantio-Obtusin docked with SARS-CoV-2 spike receptor-binding domain (PDB ID: 6m0j) using Swiss-Dock Web Server based computational tools. b. Aurantio-Obtusin (colored as per constitutive elements docked within the SARS-CoV-2 Spike receptor-binding domain (PDB ID: 6M0J) as viewed using UCSF Chimera, best pose.

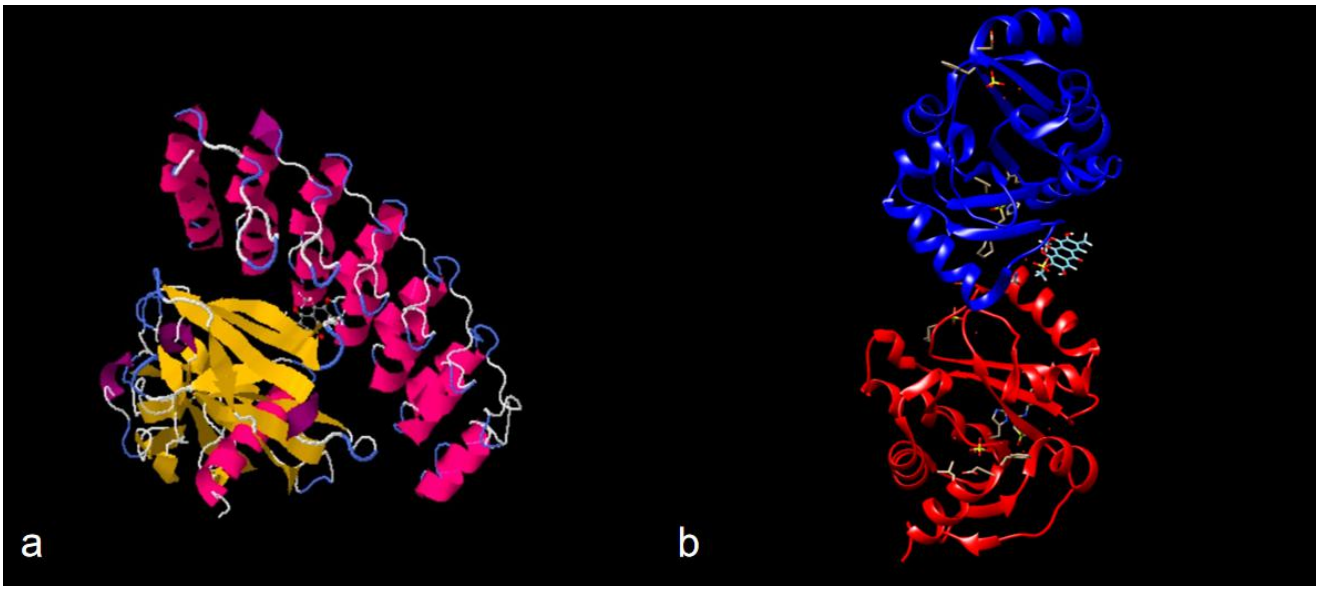

Figure 3 a. Aurantio-Obtusin docked with SARS-COV-2 PLpro (PBD ID: 6VXS) using Swiss-Dock web Server based computational tools. b. Aurantio-Obtusin (colored as per constitutive elements docked within the SARS-CoV-2 Spike receptor-binding domain (PDB ID: 6M0J) as viewed using UCSF Chimera, best pose.

Food Therapy and Health Care 2021;3(4):106–114. https://doi.org/10.53388/FTHC20210304106

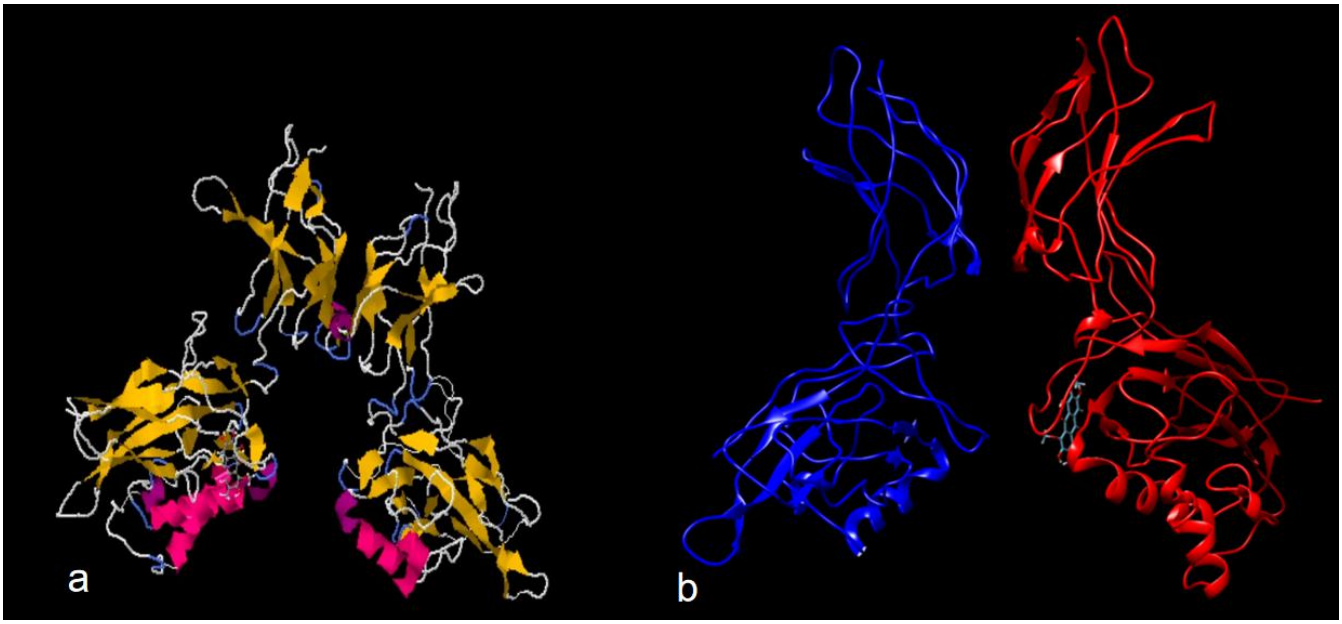

Figure 4 a. Aurantio-Obtusin docked with NF- ĸ B (PDB ID: 1VKX) using Swiss-Dock web Server based computational tools. b. Aurantio-Obtusin docked with NF- ĸ B (PDB ID:1VKX) viewed using UCSF Chimera.

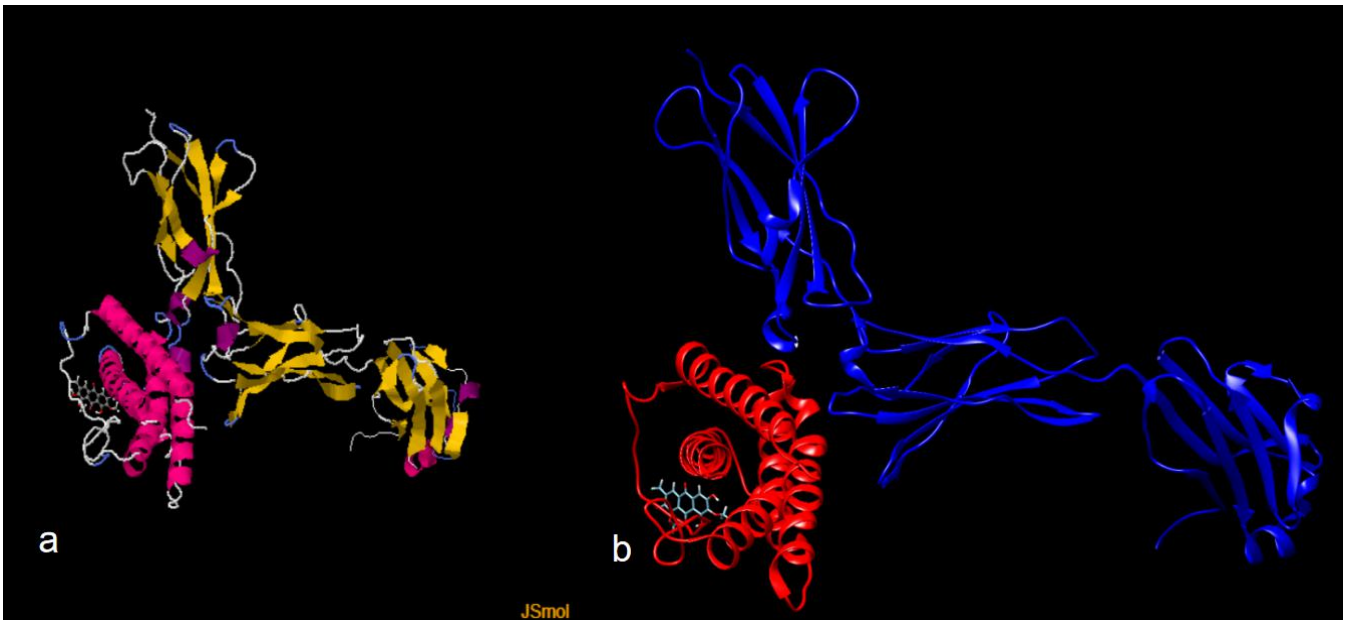

Figure 5 a. Aurantio-Obtusin docked with IL-6 (PDB ID: 1I1R) using Swiss-Dock web Server based computational tools. b. Aurantio-Obtusin docked with IL-6 receptor complex (PDB ID: 1I1R) viewed using UCSF Chimera.

Conclusions

Cassia tora Linn., a rainwater wasteland herb used in Ayurveda and Traditional Chinese Medicine; has shown a variety of medicinal benefits through various researches conducted on animals like mice, organism strains, and on certain human cells. Hence on a comprehensive review, it has proven to possess multiple pharmacological properties, such as Anti-microbial, Anti-cancer, Vasodilatory, Anti-oxidant, Hypolipidemic, Laxative, Anti-Diabetic, Hepatoprotective, Anti-Inflammatory, Immuno-stimulatory, Pesticidal, Anti-Estrogenic, Kidney protective, Cataract protective, Skin protective and Neuro-protective properties.

The significant bioactive molecules found in *Cassia tora* leaf and seed extracts like torachrysone, anthraquinones, toralactone, aloe-emodin, rhein, emodin, obtusin, aurantio-obtusin, chrysophanic acid, rubrofurasin, unglycosylated naphthalenes, etc. have shown various medicinal and non-medicinal properties through review of

literature till date since last reviewed in 2011.

Further, Aurantio-Obtusin; a bioactive molecule present in *Cassia tora* has been shown to be effective in inhibiting the S protein of SARS-CoV through binding to various protein receptors effectively and inhibiting the virus. It's also known to bind to molecules involved in the inflammation of lung tissue in a diseased state. Bioinformatics based analysis of aurantio-obtusin further revealed interesting molecular interactions *in silico* with viral as well as host components of disease progression. Further, evaluation of various bioactive ingredients of edible herb- *Cassia tora* are warranted from natural pharmacophore based drug development perspective.

References

1. Pawar, Harshal A, Priscilla MD. Cassia tora Linn.: an overview. Inter J Pharm Sci Res 2(9): 2286.
2. Sarwa, Kumar K, et al. Phytochemical and Biological Potential of Cassia tora Linn. Euro J Med Plants 2014: 946–963.
3. Oudhia, P. Phyto-sociological studies of rainy season wasteland weeds with special reference to Parthenium hysterophorus L. Asian J Microbiol Biotech Environ Sci 3 (2001): 89–92.
4. Shah, CS, Shinde MV. Phytochemical studies of seeds of Cassia tora L. and C. occidentalis L." Indian J Pharm 1969: 32: 70.
5. Kim, Myungsuk, Lim SJ, Lee HJ, Nho CW. Cassia Tora Seed Extract and Its Active Compound Aurantio-Obtusin Inhibit Allergic Responses in ige-Mediated Mast Cells and Anaphylactic Models. J Agricul Food Chem 2015: 63 (41): 9037–9046.
6. Teli, Nikhil. Bioactive Constituents , Ethnobotany and Pharmacological Prospectives Of Cassia Tora Linn. Inter J Bioassays 2016.
7. Park, Beom Y, Kim SB. Isolation and Identification of Antitumor Promoters from the Seeds of Cassia Tora. J Microbiol Biotechnol 2011, 21 (10): 1043–48.
8. CH Wu, Yen GC. Antigenotoxic Properties of Cassia Tea (Cassia Tora L.): Mechanism of Action and the Influence of Roasting Process. Life Sci 2004, 76 (1): 85–101.
9. Rejiya CS, Cibin TR, Abraham A. Leaves of Cassia Tora as a Novel Cancer Therapeutic - An in Vitro Study. Toxicol Vitro 2009: 23 (6): 1034–1038.
10. Wen CC, Shyur LF, Jan JT, Liang PH, Kuo CJ, Arulselvan P, et al. batatas, Cassia tora, and Taxillus chinensis inhibit SARS-CoV replication.
11. Zhao X, Wang Q, Qian Y, Pang L. Cassia tora L.(Jue-ming-zi) has anticancer activity in TCA8113 cells in vitro and exerts anti-metastatic effects in vivo. Oncol Letters 2013,5(3):1036–1042.
12. DOI:10.15373/2249555X/OCT2013/121Authors:Ashwini
13. Choi JS, Lee HJ, Park KY, Ha JO, Kang SS. In vitro antimutagenic effects of anthraquinone aglycones and naphthopyrone glycosides from Cassia tora. Planta medica. 1997, 63(01):11–14.
14. Kumar V, Mahdi F, Saxena JK, Singh RK, Akhter N, Ahmad S. Experimental validation of antidiabetic and antioxidant potential of T. cordifolia stems (M.): an indigenous medicinal plant. EJMR, 2017;4(2):10–15.
15. Jain SK, Bull R, Rains JL, Bass PF, Levine SN, Reddy S, et al. Low levels of hydrogen sulfide in the blood of diabetes patients and streptozotocin-treated rats causes vascular inflammation? 2010: 1333–1337.
16. Jang DS, Lee GY, Kim YS, Lee YM, Kim CS, Yoo JL, et al. Anthraquinones from the seeds of Cassia tora with inhibitory activity on protein glycation and aldose reductase. Biological and Pharmaceutical Bulletin. 2007, 30(11): 2207–2010.
17. El-Halawany AM, Chung MH, Nakamura N, Ma CM, Nishihara T, Hattori M. Estrogenic and anti-estrogenic activities of Cassia tora phenolic constituents. Chem Pharm Bulletin 2007, 55(10): 1476–1482.
18. Bhati D, Jain S. Weeds: An uncommon source of nutrients used by tribal community. Indina Ecological Soci 2015, 42(1):86–89.
19. Wu CH, Hsieh CL, Song TY, Yen GC. Inhibitory effects of Cassia tora L. on benzo [a] pyrene-mediated DNA damage toward HepG2 cells. J Agricul Food chem 2001, 49(5): 2579–2586.
20. Wu CH, Yen GC. Antigenotoxic properties of Cassia tea (Cassia tora L.): Mechanism of action and the influence of roasting process. Life Sci 2004, 76(1): 85–101.
21. Maity, TK, Dinda SC. Purgative Activity of Cassia Tora Leaf Extract and Isolated Aloe-Emodin. *Indian J Pharm Sci* 2003 65 (1): 93–95.
22. Hou J, Gu Y, Zhao S, et al. Anti-Inflammatory Effects of Aurantio-Obtusin from Seed of Cassia obtusifolia L. through Modulation of the NF-κB Pathway. Molecules 2018, 23(12): 3093.
23. Vijayalakshmi A, Madhira G. Anti-Psoriatic Activity of Flavonoids from Cassia Tora Leaves Using the Rat Ultraviolet B Ray Photodermatitis Model. *Revista Brasileira de Farmacognosia* 2014, 24 (3): 322–329.
24. Ho TY, Wu SL, Chen JC, Li CC, Hsiang CY. Emodin blocks the SARS coronavirus spike protein and angiotensin-converting enzyme 2 interaction. Antiviral Res 2007, 74(2):92–101.
25. Kwon HC, Kim TY, Lee CM, Lee KS, Lee KK. Active compound chrysophanol of Cassia tora seeds suppresses heat-induced lipogenesis via inactivation of JNK/p38 MAPK signaling in human sebocytes. Lipids Health Dis 2019, 18(1): 1–8.
26. Choi JS, Lee HJ, Park KY, Ha JO, Kang SS. In vitro antimutagenic effects of anthraquinone aglycones and naphthopyrone glycosides from Cassia tora. Planta medica. 1997, 63(01): 11–14.
27. Hyun SK, Lee H, Kang SS, Chung HY, Choi JS. Inhibitory activities of Cassia tora and its anthraquinone constituents on angiotensin-converting enzyme. Phytotherapy Research: Inter J Devoted Pharmacol Toxicol Evaluation Natural Product Derivatives 2009, 23(2): 178–184.
28. Chidume FC, Kwanashie HO, Adekeye JO, Wambebe C, Gamaniel KS. Antinociceptive and smooth muscle contracting activities of the methanolic extract of Cassia tora leaf. J Ethnopharm 2002, 81(2): 205–209.
29. Yen GC, Chung DY. Antioxidant Effects of Extracts from Cassia t ora L. Prepared under Different Degrees of Roasting on the Oxidative Damage to Biomolecules. J Agricul Food Chem 1999 19;47(4): 1326–1332.
30. Yalu H, Nagarathna PK. Cardioprotective Activity Of Leaves Of Kigelia Africana On Isoprenaline Induced Myocardial Infarction. Inter J Ayurv Pharma Res 2015.
31. Patil UK, Saraf S, Dixit VK. Hypolipidemic activity of seeds of Cassia tora Linn. J Ethnopharm 2004, 90(2-3): 249–252.
32. Awasthi VK, Mahdi F, Chander R, Khanna AK, Saxena JK, Singh R, et al. Hypolipidemic activity of Cassia tora seeds in hyperlipidemic rats. Indian J Clin Biochem 2015, 30(1): 78–83.
33. Chan SH, Koo A, Li KM. The involvement of medullary reticular formation in the hypotensive effect of extracts from seeds of Cassia tora. American J Chin Med 1976, 4(04): 383–389.
34. Lee GY, Kim JH, Choi SK, Kim YH. Constituents of the seeds of Cassia tora with inhibitory activity on soluble expoxide hydrolease. Bioorganic Medicinal Chem Letters 2015, 15(22):5097–5101.
35. Chung HS. Anthraquinones with Immunostimulating Activity from Cassia tora L. Prevent Nutrit Food Sci 2005,10(3): 267–271.
36. Cherng JM, Chiang W, Wang JH, Lin CM, Lee CY, Shih CM, et al. Anthraquinones of edible wild vegetable Cassia tora stimulate proliferation of human CD4+ T lymphocytes and secretion of interferon-gamma or interleukin 10. Food Chem 2008,107(4): 1576–1580.
37. Maity TK, Mandal SC, Mukherjee PK, Saha K, Das J, Pal M, et al. Studies on antiinflammatory effect of Cassia tora leaf extract (fam. Leguminosae). Phytother Res 1998, 12(3):221–223.
38. Hatano T, Uebayashi H, Ito H, Shiota S, Tsuchiya T, Yoshida T. Phenolic constituents of Cassia seeds and antibacterial effect of

some naphthalenes and anthraquinones on methicillin-resistant Staphylococcus aureus. Chem Pharma Bulletin 1999, 47(8): 1121–1127.
39. Chavan RT, Deshmukh VL, Kadam AS. Antibacterial Activity of Cassia Tora Leaves. Recent Research in Science and Technology 2011, 3 (5): 12–14.
40. Acharya TK, Chatterjee IB. Isolation of Chrysophanic Acid-9-Anthrone, the Major Antifungal Principle of Cassia Tora. Lloydia 1975, 38 (3): 218–220.
41. Kim YM, Lee CH, Kim HG, Lee HS. Anthraquinones isolated from Cassia tora (Leguminosae) seed show an antifungal property against phytopathogenic fungi. J Agricul Food Chem 2004, 52(20): 6096–6100.
42. Mukherjee PK, Saha K, Saha BP, Pal M, Das J. Antifungal activities of the leaf extract of Cassia tora Linn. (Fam. Leguminosae). Phytother Res 1996, 10(6): 521–522.
43. Dharmendra D, et al. Antimicrobial Activity of Methanolic Extracts Of Cassia tora root." Int J Pharm Biol Arch 2010: 569–571.
44. Khalifa SAM, Yosri N, El-Mallah MF, et al. Screening for natural and derived bio-active compounds in preclinical and clinical studies: One of the frontlines of fighting the coronaviruses pandemic. Phytomed 2021,85:153311.
45. SL D, Khadabadi SS., Kamdi KS, Ingle VP. In vitro anthelmintic activity of Cassia tora. Vitro 2009, 1(2):177–179.
46. Gaikwad SA. Phytochemical investigation of bioactive Emodin and quercetin in Cassia fistula and Cassia tora plant parts by HPTLC. J Pharmacogn Phytochem 2018,7: 892–897.
47. Baskar K, Ignacimuthu S. Antifeedant, larvicidal and growth inhibitory effects of ononitol monohydrate isolated from Cassia tora L. against Helicoverpa armigera (Hub.) and Spodoptera litura (Fab.)(Lepidoptera: Noctuidae). Chemosphere 2012, 88(4): 384–388.
48. Sreelakshmi, V, Abraham A. Protective Effects of Cassia Tora Leaves in Experimental Cataract by Modulating Intracellular Communication, Membrane Co-Transporters, Energy Metabolism and the Ubiquitin-Proteasome Pathway. Pharma Biol 55 (1): 1274–1282.
49. Jang DS, Lee GY, Kim YS, Lee YM., Kim CS, Yoo JL et al. Anthraquinones from the seeds of Cassia tora with inhibitory activity on protein glycation and aldose reductase. Biolo Pharma Bulletin 2007, 30(11): 2207–2210.
50. Rajan A, Vetrivel et al. Hepatoprotective effects of Cassia tora on CCl 4 induced liver damage in albino rats. Indian J Sci Technol 2009: 41–44.
51. Dhanasekaran M, Ignacimuthu S, Agastian P. Potential hepatoprotective activity of ononitol monohydrate isolated from Cassia tora L. on carbon tetrachloride induced hepatotoxicity in wistar rats. Phytomed 2009, 16(9): 891–895.
52. Fathalla N, Bishr M, Singab AN, Salama O. Phytochemical and biological evaluation of Cassia tora, L. seeds. J Pharm Biol Sci 2015, 10(1):1–8.
53. Jung DH, Kim YS, Kim NH, Lee J, Jang DS, Kim JS. Extract of Cassiae Semen and its major compound inhibit S100b-induced TGF-β1 and fibronectin expression in mouse glomerular mesangial cells. Europ J Pharmacol 2010:641(1): 7–14.
54. Park SI, Yun HC, Kang SW, Kim SK, Lee H, Park MS, et al. Effect of Seed of Cassia tora Extract in the Prevention of Remote Renal Reperfusion Injury. In Transplant Proceed 2019:51(8): 2833–2837
55. Ravi SK, Narasingappa RB, Joshi CG, Girish TK, Vincent B. Neuroprotective effects of Cassia tora against paraquat-induced neurodegeneration: relevance for Parkinson's disease. Natural Product Res 2018, 32(12): 1476–1480.
56. Park TH, Kim DH, Kim CH, Jung HA, Choi JS, Lee JW, et al. Peroxynitrite scavenging mode of alaternin isolated from Cassia tora. J Pharm Pharmacol 2004, 56(10): 1315–1321.
57. Chethana KR, Senol FS, Orhan IE, Anilakumar KR, Keri RS. Cassia Tora Linn.: A Boon to Alzheimer's Disease for Its Anti-Amyloidogenic and Cholinergic Activities. Phytomed 2017, 33: 43–52.
58. Lee SJ, Jeong D, Park WK, Kong JY, Choi G, Kim H, Kang S, Cho H. Screening of Kit inhibitors: suppression of Kit signaling and melanogenesis by emodin. Phytother Res 2010, 4(2): 308–312.
59. Hirano T, Murakami M. COVID-19: a new virus, but a familiar receptor and cytokine release syndrome. Immunity 2020: 52(5):731–733.
60. Walls AC, Park YJ, Tortorici MA, Wall A, McGuire AT, Veesler D. Structure, function, and antigenicity of the SARS-CoV-2 spike glycoprotein. Cell 2020, 181(2): 281–292.
61. Kim YS, Jung DH, Sohn E, Lee YM, Kim CS, Kim JS. Extract of Cassiae semen attenuates diabetic nephropathy via inhibition of advanced glycation end products accumulation in streptozotocin-induced diabetic rats. Phytomed 2014: 21(5): 734–739.