THERAPEUTIC POTENTIAL OF THE PHYTOCHEMICALS IN CASSIA OCCIDENTALIS-A REVIEW

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ABSTRACT
This article reviews the therapeutic potential of various phytochemicals present in Cassia occidentalis Linn, a perennial plant of leguminosae family, which has been traditionally used as a medicine against various diseases. It is commonly found in India and in many tropical countries. This plant has many pharmacological applications which are attributed to the presence of active phytochemicals in leaves, stem, roots and seeds. Phytochemicals present in Cassia Occidentalis Linn such as anthraquinones, anthraquinone glycosides, flavanoids and physterols show analgesic, antipyretic, antimalarial, antioxidant, anticancer activity etc. These phytochemicals are good reducing agents in the formation silver nano particles also. However, the presence of trace elements demands attention due to their toxicity on continuous use.

KEY WORDS: Cassia occidentalis Linn, Phytochemicals, silver nano, trace metals.

INTRODUCTION
Cassia is a genus of flowering plants in the legume family, Fabaceae and the subfamily Caesalpinioideae. Species are known commonly as cassis. There are hundreds of Cassia species[1]. Among them, Cassia occidentalis Linn is an annual or perennial plant which is used in several traditional medicines to cure various diseases[2]. It is distributed throughout India and in most tropical countries[3]. It is known by different names[4] such as, Badikanodi, Chakunda and Kasonda in Hindi, Coffee Senna, Foetid Cassia, Negro Coffee, Rubbish Cassia, and Stinking Weed in English, Kasamarda in Sanskrit, Chakundra Talka in Rajasthani, Payaverai, and Nattam Takarai, Payaveri in Tamil.

It is worth to mention that, different parts of the plant have similar properties such as purgative, tonic, febrifugal, expectorant and diuretic property. The plant is used to cure sore eyes, haematuria, rheumatism, typhoid, asthma and disorders of hemoglobin. Its effective use for curing leprosy has also been reported. A decoction of the plant is used in hysteria, in dysentery and other stomach troubles and also as an application to sores, itch and inflammation of the rectum. The plant is employed in dropsy and as a vermifuge, anticonvulsant and used against chicken pox[5-6]. Along with other plants, it is made into an ointment used for skin diseases. The herb is reported to be used as condiment and in perfumery.

The herb forms an ingredient of the patented indigenous herbal drug Liv 52”(produced by Himalayan Drugs, India) which shows marked effect in the early cases of hepatic cirrhosis having steatorrhoea. Liv 52 reduced the toxicity of cadmium and beryllium in experimentally infected rats with SFV (Semiliki Forest Encephalitis Virus)[5]. In Unani and Ayurvedic medicine, the pods and leaves are used as great tonic as an infusion. Women who nurse develop milk in copious quantities after consuming extracts of this plant. Besides this, it is used to treat colitis and constipation. Cloves and ginger is added to mark the odor that is disagreeable. It is effective in treating vomiting, hiccups, cholera, gout, biliousness, and jaundice. To dye the hair black, it is used with henna leaves[7]. The young leaves are eaten alone or cooked along with unripe pods and eaten with rice. The leaf when eaten is reported to act as a prophylactic against leucorrhoea. Fresh leaves poured with salt and onions are applied as a poultice to guinea worm sores to extrude the worms. They are used in the inflammatory swelling, rheumatism, wounds, sprains and wrenches and also given in jaundice pleurisy, head ache and toothache. A paste of the leaves with calcium hydroxide is applied on abscesses for quick opening and pus clearance. The leaf paste is also applied externally for bone fracture. The leaves are used in foot and mouth disease of cattle. Their extract exhibits activity against earthworms[8].
In Senegal, the leaves are used to protect cowpea seeds, Vigna unguiculata Linn (Walpers) against callosobruchus maculatus (coleoptera: Bruchidae). Both fresh and dry leaves as well as whole and ground seeds had no contact toxicity on the cowpea beetle. In contrast, seed oil induced an increase in mortality of C. maculatus eggs and first larval in star at the concentration of 10ml/kg cowpea.8

The seed is bitter and has tonic, febrifugal and purgative properties. It is considered as blood tonic and excellent diuretic. Seeds are useful in cough and whooping cough, convulsions and in heat diseases. Their powder is externally applied in cutaneous diseases and eruptions. The extracts showed positive response on guinea pig ileum, rat uterus, rabbit-heart and depress or effect on blood pressure of dogs and also activity against earthworms3 and are used to treat hypertension16. The seeds are used as a cure of convulsion in children and are used in West Africa to prepare a beverage which serves as a substitute for coffee10.

The roots are also bitter, purgative, anthelmintic and diuretic. Roots are given with lime to treat dysentery and diarrhoea associated with malaria. They are used for relief in cramps, itches and sore throat. The root bark is also used to cure malaria. Root bark decoction is an effective remedy against gonorrhea and hepatic malfunction. The Indians use the roots to treat fungal infections of the skin11. The medicinal activity of this plant is due to the presence of phytochemicals whose properties are analyzed in pharmacological investigations. Pharmacological investigations have revealed the presence of several therapeutic activities - antioxidant, analgesic, anti-inflammatory, hepatoprotective, anti-malarial, anti-diabetic, anticancer, antidepressant11, nephroprotective13, antimicrobial13, anti-fertility14, anti-plasmodial15, anti-mutagenic16,17, anti-allergic and anti-lipid peroxidation18 activities. These activities are mainly due to the presence of organic compounds. The presence of inorganic substances were reported to enhance the activities of these natural organic compounds19. The presence of trace elements at low concentrations in leaves increased attention due to their toxicity20.

**Phytochemical constituents in leaves, seeds, stem and flowers** are13,21-32

**Anthraquinones and their glycosides:** Chrysophanol, Chrysophanol acid, Chryso-obtusin, Aurantio-obtusin, Chrysoriel, Obtusifolin, Obtusin, Emodin, Physcion, 4,4',5,5'-tetratetrahydroxy-2,2'‘-dimethyl-1,1' biantraquinone, germichryson, Occidentalins A&B, 1,8-dihydroxy-2-methyl anthraquinone, Rhein, Aloe emodin, Occidental-I, Occidental-II, α-hydroxy anthraquinone, Pinulin or Cassialin, Islandicin, Helmithosporin, Xanthorinel, Matteucinol-7-rhamnoside, Jaceind-7-rhamnoside, Questin, Torosachrysone, Germitorosone, methyl germitorosone, Helminthosporin, N-methyl morpholine, Singueanol I and Sennosides A,B,C, and Chysarobin.

**Glycosides:** 7-O Methyl-quercetin and 3,5,3’-trimethoxy quercetin: O-alpha-d-galactopyranosyl-(1-6)-beta-d mannopyranosyl, O-alpha-d-mannopyranosyl- (1-4)-o-beta-d-mannopyranosyl

**Flavanoids:** Torosa flavon B, Cassia Occidentalin A, B, C, Apigenin, Kaempferol

**Poly Saccharides:** Galactomannan, galactopyranosyl

**Fatty acids:** Lignoceric acid, Linoleic acid, Oleic acid

**Phenantheracene derivative:** Campestero

**Phytosterol:** Sitosterols such as β-sitosterol-α-glucoside, Alpha-3-sitosterol,

**Sugar alcohol:** Mannitol

**Essential Oils**

Trace metals identified are Calcium, Copper, Iron, Magnesium, Mangenese, Potassium, Sodium, Zinc, Chromium, Nickel, Cobalt, Lead, Aluminium, Rubedium, Lanthanum, Scandium, Samarium, Thorium20,31 and Silver10.

**Toxic Effects**

Acute toxicity test was conducted on *Cassia occidentalis Linn* and found that this plant did not show any hazardous symptoms or death32. But the following symptoms occur in animals when fed on excessive amounts of the plant: lack of coordination, reluctance to move, anorexia, muscle weakness, diabetes, muscle tremors, body weight loss and death. Those ingesting the seeds show profound skeletal muscle degeneration also degenerative myopathy of the cardiac muscle, congestion and pulmonary oedema and necrosis. In human indigestion of raw seeds will cause gastro-intestinal symptoms. Roasted seeds do not seem to cause these symptoms35. The toxic compounds implicated for poisoning are chrysalobrin (3-methyl-1,8,9- anthracenetriol), emodin (6-methyl-1,3,8-trihydroxyanthraquinone) and a lectin (carbohydrate-binding proteins).

The study of sub-acute oral administration of *Cassia occidentalis Linn* during pregnancy in female wistar rats found that there was no statistically significant changes between control and test groups with respect to fetuses, placentae and ovaries weights; number of implantation and resorption sites; number of corpora lutea in the ovaries and pre- and post-implantation loss rates, in both does of (250 and 500mg/kg) Cassia occidentalis Linn. This is enough to put a cautionary note on its use during pregnancy36.

**Pharmacological Activities**

**Analgesic and Antipyretic activities:** Ethanolic and aqueous extract of leaves (150 and 300 mg / kg) exhibited significant dose - dependent antiinocicptive and antipyretic effects in rats/mice models. Highest inhibition dose was found to be 300 mg/kg. The report clearly mentioned that both the ethanolic and water
extracts of *Cassia occidentalis* Linn showed significant effect on pyrexia induced by yeast\[^{37}\].

**Antioxidant Activity:** The antioxidant and free radical scavenging activities of ethanolic extract of *Cassia occidentalis* Linn leaves (COLEX) is compared with the standard antioxidants BHA and BHT using four different methodologies including total reducing capability, total antioxidant activity, DPPH radical and hydrogen peroxide scavenging assays. In addition the effect of COLEX on the sodium arsenate induced hepato toxicity in the male wistar rats are determined. This study revealed that ethanolic extract of *Cassia occidentalis* Linn leaves possesses potent antioxidant and free radical scavenging activities\[^{38}\].

The antioxidant potency of sequential organic and aqueous leaf extract of *Cassia occidentalis* Linn was investigated employing various established in vitro systems such as nitric oxide scavenging (NOS) activity, β-carotene linoleic acid model system hydroxyl radical scavenging (ihrs) activity, reducing power, metal chelating activity (MCA) and super oxide radical scavenging (SRS) activity. The aqueous extract of the

leaves of *Cassia occidentalis* Linn was found to be most effective against free radical followed by methanolic, chloroform, petroleum ether and benzene extracts respectively\[^{39}\].

The phytochemical screening of *Cassia occidentalis* Linn was performed in petroleum ether, chloroform and methanolic extracts. The chloroform and methanolic extracts of both flower and seed were found to contain flavonoids, alkaloids, phenolics/tannins, steroids, glycosides and anthraquiones. The antioxidant potential of flowers and seeds in different solvent extracts were evaluated by various biochemical assays namely, DPPH (2, 2'- diphenyl-1-picyrlhydrazyl) radical scavenging activity, reducing power activity. Their SC50 and EC50 values were determined to evaluate the therapeutic potential, in which seeds were found to have higher antioxidant activity revealed by lower SC50 and EC50 value. The total phenol, flavonoid, flavonol and tannin content were determined for both parts to study the free radical scavenging property. The seeds were found to have higher antioxidant activity when compared to flowers in various solvent extracts indicating their pharmacological property(Figure 1, Figure 2)\[^{40}\].

**Figure 1.** Nitric oxide radical scavenging activity of methanol extracts of leaves, stem and seeds of *Cassia occidentalis*\[^{40}\]

**Figure 2.** Hydroxyl radical scavenging activity of methanol extracts of leaves, stem and seeds of *Cassia occidentalis* \[^{40}\]
In vitro antioxidant activity of methanol extract of *Cassia occidentalis* Linn seeds was determined by DPPH free radical scavenging (Figure 1), FRPA, Lipid peroxidation by thiobarbituric acid assay methods (Figure 3). The analysis had shown the maximum percentage inhibition in case of DPPH method as 66.53% at 160µg/ml and 61.07% in lipid peroxidation at 1000µg/ml. Total phenolic content estimation was done by using Folin-Ciocalteu reagent and was found to be 0.75% w/w. Their study revealed that the methanol extract of seeds has antioxidant potential and represent a potential source of medicine (Figure 3, Figure 4, Figure 5)\[41\].

**Anticancer activity:** Aqueous and hydro-alcoholic extracts of whole plant had been shown to cause growth inhibition of eight human cancer cell lines viz. HCT-15, SW-620, COLO-205 (colon); OVCAR-5 (ovary), PC-3 (prostate), HOP-62 (lungs), MCF (breast) and SiHa (cervix)\[42\].

**Anti-inflammatory and Anti-allergic activities:** The anti-allergic, anti-inflammatory and anti-oxidant properties of *Cassia occidentalis* Linn whole plant was investigated\[18\]. Effects of *Cassia occidentalis* Linn on rat mast cell degranulation inhibition and human red blood cell membrane stabilization were studied in vitro following standard methods. The anti lipid peroxidant effect was also studied in vitro. Results of this study indicated that *Cassia occidentalis* Linn inhibited HRBC membrane thereby alleviating immediate hyper sensitivity besides showing antioxidant activity\[18\]. The extract of the leaves of *Cassia occidentalis* Linn obtained by cold extraction using a mixture of equal proportions of petroleum ether, ethyl acetate and methanol was chosen for pharmacological screening. Carrageenan-induced rat hind paw edema was used as the animal model for inflammation study and the inhibition of carrageenan-induced inflammation by the extract could be due to the inhibition of the enzyme cyclooxygenase and subsequent inhibition of prostaglandin synthesis. This study on extract of *Cassia occidentalis* Linn has demonstrated that this plant has significant analgesic and anti-inflammatory properties\[43\].

The anti-inflammatory and antipyretic activities of the methanol fraction and its pure compound chrysophanol of *Cassia occidentalis* Linn was analysed in male albino wistar rats. Paw edema was produced by subplantar injection of carrageenan, cotton pellet granuloma was produced by implantation of 30mg sterile cotton in groin region. The results showed that the extract and chrysophanol significantly inhibited inflammation and
Antimalarial activity: The isolated phytochemicals of *Cassia occidentalis* Linn was evaluated and characterized by using various chromatographic techniques and spectroscopical analysis. The in vitro antimalarial assay was carried out in 96 well microtitre plates according to the microassay protocol of Rieckmann and co-workers with minor modifications. The results showed that the leaves have anti-malarial activity due to the presence of quinones.[46]

The ethanolic, dichloromethane and lyophilized aqueous extracts of *Cassia occidentalis* Linn root bark, Morinda morindoides leaves and whole plants of Phyllanthus niruri were evaluated for their antimalarial activity in vivo, in 4-day, suppressive assays against Plasmodium berghei ANKA in mice. The extracts produced significant chemosuppressions of parasitemia with 200 mg/kg dose when administered orally. *Cassia occidentalis* Linn was found to be potential with 60% chemosuppression. They also found that the ethanolic extract is more active than the lyophilized aqueous extract cassia occidentalis leaf extract with ethanol and chloroform was found to possess better antimalarial activity.[47,48]

Anti-bacterial activity: The ethanolic and aqueous extract of the leaves of *Cassia occidentalis* Linn revealed the presence of tannins, saponins, cardiac glycoside, terpenoids and anthraquinones. The extracts were used to carryout anti microbial screening in vitro on staphylococcus aureus, E-coli, salmonella typhi and pseudomonas aeruginosa. These phytochemicals make the extract anti-bacterial anti-fungal[49]

Leaves of *Cassia occidentalis* Linn were extracted with ethanol and water. The extracts were used to carry out antimicrobial screening in vitro on staphylococcus aureus, pseudomonas aeruginosa, Escherichia coli, salmonella typhi, shigella spp. Chromatographic separation was carried out on the active extracts, and the efficacy of the resulting fractions was tested against the susceptible organism. Some of the extracts indicated significant inhibitory activity against the tested organisms. General phytochemical screening was done on the ethanol, water extracts and fractions. Ethanol extract revealed the presence of tannins, saponins, cardiac glycoside, terpenoids and anthraquinones. This result might explain the ethnomedical use of the plant for the treatment of dysentery, gastro internal disorder, constipation and Typhoid fever.[50]

The flower extract of *Cassia occidentalis* Linn is used to evaluate the in-vitro antibacterial activity. The clinical bacterial isolates, Klebsiella pneumoniae, Staphylococcus aureus, Streptococcus pneumoniae and Pseudomonas aeruginosa were subjected to antibacterial susceptibility test using agar well diffusion method. The phytochemical analysis of the flower extracts revealed the presence of tannin, flavonoid, anthraquinone, saponin, carbohydrates, and cardiac glycoside. *Cassia occidentalis* Linn flower extract might therefore be used to treat Klebsiella associated illness such as pneumonia and bronchitis[51].

Minimum Inhibitory Concentration (MIC) of the extracts was performed and the zone of inhibition was studied to evaluate the plant’s antibacterial and antifungal activities. The results of MIC study revealed the antimicrobial activity of the extracts against the strains of microorganisms between concentration ranges of 25 and 450ug/ml. The results of zone of inhibition study revealed that the plant possess antimicrobial activity, more susceptible to gram positive than gram negative bacteria in a concentration dependant manner[52].

Different organic and aqueous extracts of leaves of *Cassia occidentalis* Linn (Caesalpiniaceae) were screened for their antimicrobial activity against seven human pathogenic bacterial and two fungal strains by disk diffusion assay. The pattern of inhibition varied with the solvent used for extraction and the microorganism tested. Among these extracts, methanol and aqueous extracts showed significant antimicrobial activity against most of the tested microbes. The most susceptible microorganism was P. aeruginosa (18mm zone of inhibition in aqueous extract) followed by P. mirabilis (15 mm zone of inhibition in methanol extract) and Candida albicans (8 mm zone of inhibition in methanol extract).[53]

The methanol portion was subsequently partition with chloroform, ethyl acetate and n-butanol. The phytochemical studies of the partition portion were done using standard protocols.

The bacteria used for the research work include Staphylococcus aureus, Pseudomonas aeruginosa, Klebsiella spp, Escherichia coli, Bacillus subtilis and the fungi used for the research work was Candida albicans. The zone of inhibition (ZI), Minimum Inhibitory Concentration (MIC) and Minimum Bactericidal Concentration (MBC) were determined. The antimicrobial screening revealed that the extract exhibited varying activity against different microbes. These activities observed could be attributed to the presence Active metabolites contained in the extract[54].

Anti-diabetic and Hepatoprotective activities: The methanol fraction of *Cassia occidentalis* Linn leaves was tested against streptozotocin-induced diabetic rats. Experiment group rats were induced diabetes by a single intraperitoneal injection of streptozotocin (STZ). Treatment with COLMF at different doses and times following in normal and diabetic rats significantly reduced the blood glucose level to normal in diabetic rats[55].
Aqueous extract of *Cassia occidentalis Linn* exhibited significant antihyperglycemic activity in normal and alloxan-induced diabetic rats. They also showed improvement in parameters like body weight and serum lipid profiles as well as histopathological studies showed regeneration of β-cells of pancreas and so might be of value in diabetes treatment \[56\].

Acute and chronic treatment of the aqueous extract of aerial parts (leaves, stem and seeds of the plant) of *Cassia occidentalis Linn* in alloxan-induced diabetic rats resulted in a significant decrease in the elevated blood glucose levels as compared to the control, there was significant reduction in blood glucose level in the group treated with glibenclamide. The results showed that blood glucose level gets decreased after varying the dose level. Thus the findings confirmed that level of blood glucose gets normal in dose-dependent manner \[57\].

The hepatoprotective effect of the *Cassia occidentalis Linn* is analysed in carbon tetrachloride induced liver damage in albino rats. The roots were found to be rich in antioxidants. Liver damage in rats were induced by carbon tetrachloride. To find out the hepatoprotective activity, the aqueous extract of the plant root samples were administrated to rats for 15 days. The serum marker enzymes Aspartate transaminase, Alanine transaminase and Gama Glutamyl were measured in experimental animals. The increased enzyme levels after liver damage with carbon tetrachloride were nearing to normal value when treated with aqueous extract of the root samples \[58\].

The hepatoprotective potentials of aqueous leaf extract of *Cassia occidentalis Linn* on paracetamol-induced hepatotoxicity in adult Wistar rats is examined. Hepatotoxicity was induced in the test groups via oral administration of paracetamol. Using standard laboratory procedures, the livers were harvested, histologically processed, and examined. The results showed that the aqueous leaves extract of *Cassia occidentalis Linn* may be hepatoprotective against hepatotoxicity \[59\].

The hepatoprotective effects and anti-oxidant activities of methanol leaf extract of *Senna occidentalis* was examined against aceterminophen-induced hepatic injury in rats. Acute toxicity test was done in rats orally. Hepatoprotective activity of the extract was investigated in rats challenged with aceterminophen. Silymarin was used as positive control. Serum (alanine aminotransaminase) ALT, (aspartate aminotransferase) AST, (alkaline phosphatase) ALP, total bilirubin and total protein levels were assayed. The findings suggest that the methanol leaf extract of *saccia occidentalis* may be useful in the protection of the hepatocytes from toxins \[60\].

**Anti-fertility activity:** Traditional physicians in and around Kotagiri village near Ootacamund, use a mixture of powdered roots of *Cassia occidentalis Linn*, *Derris brevipes* variety coriacea and *Justicia simplex* to control female fertility. A mixture of powdered roots of these three plants, powdered root of *Derris brevipes* variety coriacea and its ethanolic extract were screened for antifertility activity in proven fertile female rats. The rats, which continued their pregnancy, did not deliver any litters after their full term. Hence, the combined antifertility (anti-implantation and abortifacient) activity of the ethanolic extract was 100%. The results suggest that the ethanolic extract possesses more abortifacient type effect than the anti-implantation activity \[14,61\].

**Nephroprotective Activity:** Lipid peroxidation may occur in the course of gentamicin administration, giving rise to free radicals which are highly toxic to tissue. The nephroprotective activity of the hydroalcoholic extract of *Cassia occidentalis Linn* was tested against gentamicin induced nephrotoxicity in rats. The degree of protection was determined by estimating urinary creatinine, urinary glucose, urinary sodium, urinary potassium, blood urea, serum creatinine levels and body weight of the animals. The In-vivo antioxidant activity was determined by estimating the tissue levels of GSH, SOD, catalase and lipid peroxidation. The treatment with the extract markedly reduced gentamicin induced elevation of urinary sodium, potassium electrolytes, urinary glucose, blood urea and creatinine levels \[12\].

**Wound-Healing activity:** Chrysophanol extracted from the leaves of *Cassia occidentalis Linn* had shown a wound healing effect in albino Wistar rats. This compound was able to cause decrease in the period of epithelialization and increase rate of wound contraction \[62\].

**Trace metals** such as chromium, copper, nickel, cobalt, iron, manganese, zinc, and lead were determined using atomic absorption spectroscopy(AAS) after ashing the samples in a muffle furnace at $550^\circ C$ at 4 hours. Their concentration in different sites had showed that the medicinal plants should be regularly monitored and checked before use for medication as net accumulation can be detrimental to health \[60\].

Assessment of oxidative stress levels and tissue concentrations of elements in these plants growing wild on fly ash basins is critical for realistic hazard identification of fly ash disposal areas. Plants growing on the fly ash basin had significantly high foliar concentration of As, Ni, Pb and Se and low foliar concentration of Mn and Fe compared to the plants growing on the reference site. The plants inhabiting the fly ash basin showed signs of oxidative stress and had elevated levels of lipid peroxidation, electrolyte leakage from cells and low levels of chlorophyll a and total carotenoids compared to plants growing at the reference site. The levels of both protein thios and nonprotein thios were elevated in plants growing on the fly ash basin compared to plants growing on the reference site \[63\].
The 5 minerals namely; lead (Pb), cadmium (Cd), aluminum (Al), mercury (Hg), and arsenic (As) in 10 common medicinal plants (Alchornea cordifolia, Alstonia boomei, Cassia alata, Cassia occidentalis, Cynbogopon citratus, Moringa olefera, Ocimum gratissimum, Paullinia pinnata, Rauwolfia vomitoria, and Taraxacum officinale leaves) are analyzed used in the treatment, prevention, and management of diseases and sampled from 5 different geographical locations in Ghana. This may help understand the importance of location in collection and ultimately heavy metal toxicity of medicinal plants[64].

The contents in Senna occidentalis Linn can be assessed using neutron activation analysis (NAA). The analysis shows that, Al, Ca, Fe, Na and K are the major components, followed by Mn, Zn and Rb. The traces of Co, Rb, La, Sc, Sm and Th are also identified. As it contains, toxic metals (such as As) at low levels, prolonged consumption of the plant may lead to their bioaccumulation. The pattern of bioaccumulation of the elements does not follow any particular trend among the different parts of the plant[65].

CONCLUSION

Cassia occidentalis Linn plant has remarkable medicinal applications due to various active phytochemicals present in it, which are experimentally verified. However, prolonged consumption of the plant is not advised because of the presence of toxic metals at low levels, which may lead to its bioaccumulation.

REFERENCE

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