

Cassia fistula Linn: Potential candidate in the health management

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ABSTRACT

Cassia fistula Linn is known as Golden shower has therapeutics importance in health care since ancient times. Research findings over the last two decade have confirmed the therapeutics consequence of *C. fistula* in the health management via modulation of biological activities due to the rich source of antioxidant. Several findings based on the animal model have confirmed the pharmacologically safety and efficacy and have opened a new window for human health management. This review reveals additional information about *C. fistula* in the health management via *in vivo* and *in vitro* study which will be beneficial toward diseases control.

Key words: Antioxidant activity and health management, anti-tumor activity, *Cassia fistula*

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INTRODUCTION

The use of plants and their constituents in primary health care has ancient history as old as human beings. Various medicinal plants has proven therapeutics implication in the health management via antioxidant, anti-inflammatory, anti-diabetic, and other biological activities^[1-3]. The consequence of herbs has been also stated in the different religious book. In Islam, the importance of herbs in health care has been discussed in details and Prophet Mohammed (Peace Be Upon Him) recommended several plants fruits and seed in the cure of various diseases.^[4] *Cassia fistula* Linn, belongs to family Caesalpiniaceae commonly known as Amulthus/Indian laburnum has been widely used in different types of traditional medicines including Ayurveda, Unani and Chinese in the treatment and prevention of diseases. *C. fistula* is native to South Asia and also cultivated in other part of the world it contains various types of constituents such as rhein, triterpenes, sugar, and potassium. Studies based on the animal model have confirmed that *C. fistula* and their constituents shows a role in diseases management via modulation of biological activities. A range of studies reported the

activity *C. fistula* as antifertility^[5] and anti-microbial.^[6,7] A study results concluded that the aqueous extract of fruit pulp of *C. fistula* possesses significant hepatoprotective activity.^[8] Earlier finding has shown that *C. fistula* bark extracts showed significant radical scavenging via inhibiting lipid peroxidation initiated by CCl₄ and FeSO₄ in rat liver and kidney homogenates.^[9] A study was performed to evaluate the potential of *C. fistula* to treat the infected wound and results confirmed that *C. fistula* treated rats showed, better wound closure, improved tissue regeneration at the wound site.^[10] This review summarized the role of *C. fistula* in the health management via antioxidant, anti-inflammatory, anti-diabetic, and other various biological activities.

BOTANICAL INFORMATION OF CASSIA FISTULA

The botanical name of is *C. fistula*, and it belongs to the kingdom plantae and family fabacea. It is also known as golden shower and Indian laburnum. *C. fistula* is medium-sized tree up to 24 m in height as well as 1.8 m in girth and it is cultivated in almost all over India^[11] *C. fistula* is a deciduous tree with greenish gray bark, leaves are compound, leaflets are each 5–2 cm long pairs^[12] and it contains around three to eight pairs of opposite leaflets. It produced fowlers in golden yellow color and shows showering bunch of up to 40 cm long earning its popular names golden shower tree.^[13] Detailed botanical classification of *C. fistula* is given below.^[12]

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Botanical information of *Cassia fistula*

- Kingdom: Plantae
- Subkingdom: Tracheobionta
- Super division: Spermatophyta
- Division: Magnoliophyta
- Class: Magnoliopsida
- Sub class: Rosidae
- Order: Fabales
- Family: Fabaceae
- Genus: *Cassia*
- Species: *Fistula*.

Chief ingredients/isolated compound of *Cassia fistula*

Cassia fistula shows a pivotal role in diseases prevention due their valuable ingredients. Some of the constituents show role as antimicrobial and antioxidant, and other types has therapeutic implications in cancer prevention via modulation of genetic pathways. Part of plants such as stem, leaf, and flower contains different types of constituents, and such types of constituents have proven therapeutics role in health care [Table 1]. Previous finding has reported that stem bark of *C. fistula* is a chief source of lupeol, β -sitosterol, and hexacosanol.^[14] Fruits and flower of *C. fistula* are a source of important ingredients, and those ingredients show role in health management. A compound such as 1,8-dihydroxy-3-anthraquinone derivative isolated from the fruit pulp^[15] and compound isolated from the flowers are kaempferol, leucopelargonidin tetramer, rhein, fistulin, and triterpenes.^[16] An important study reported that seeds of *C. fistula* are rich in glycerides with linoleic, oleic, stearic, and palmitic acids as chief fatty acids and also contains traces of caprylic and myristic acids.^[17]

The compounds such as Heptacosanyl-5-hydroxypentadec-2-enoate and octacosan-5, 8-diol isolated from the leaves of *C. fistula*^[18] and valuable constituents present in pulp such as high concentration of soluble sugar, sucrose, fructose and glucose, and good source of macromineral elements, calcium and potassium.^[19] Other compounds isolated from the seeds of *C. fistula* are 5-(2-hydroxyphenoxymethyl)furfural, (2'S)-7-hydroxy-5-hydroxymethyl-2-(2'-hydroxypropyl)chromone, benzyl 2-hydroxy-3,6-dimethoxybenzoate, and benzyl 2 β -O-D-glucopyranosyl-3,6-dimethoxybenzoate, together with other compounds, 5-hydroxymethylfurfural, (2'S)-7-hydroxy-2-(2'-hydroxypropyl)-5-methylchromone, and two oxanthraquinones, chrysophanol and chrysophanein.

hydroxy-5-hydroxymethyl-2-(2'-hydroxypropyl)chromone, benzyl 2-hydroxy-3,6-dimethoxybenzoate, and benzyl 2 β -O-d-glucopyranosyl-3,6-dimethoxybenzoate, together with other compounds, 5-hydroxymethylfurfural, (2'S)-7-hydroxy-2-(2'-hydroxypropyl)-5-methylchromone, and two oxanthraquinones, chrysophanol, and chrysophanein.^[20] A numerous valuable constituents present in different parts of the plants and such types of ingredients shows a role in health management. Anthraquinones such as rhein, chrysophanol, and physcion were isolated from the leaves of the *C. fistula*^[21] and galactomannan constitutes of different type of sugar moieties are also reported from the seeds.^[22]

Pharmacological activities of *Cassia fistula*

Antioxidant activity

Antioxidants are the compounds that neutralize the attack of free radicals and, therefore, reduce the risk of disorders.^[23] Antioxidant activity of natural source has proven therapeutics role in the prevention of various pathogenesis due to the rich source of antioxidant. Medicinal plants contain several valuable ingredients such as tocopherol, flavonoids, and polyphenols, some essential amino acids and all these constituents show a role in health care. Phenols especially bioflavonoids are a good source of antioxidant and shows valuable role as free radical scavengers.^[24-26] The importance of *C. fistula* in diseases control has ancient background due to high sources of antioxidants. A recent study was performed to evaluate the antioxidant potential and protective effect of *C. fistula* Linn. on hydrogen peroxide-induced oxidative damage in erythrocytes and results confirmed that *C. fistula* ethanolic extract showed high antioxidant activity and as more than 90% protection of erythrocytes whereas *C. fistula* aqueous extract showed 75% antioxidant and protective activity.^[27]

Another study was performed to analyze the antioxidant activity based on *C. fistula* bark, stem, leaf, and root, and results showed that bark extracts from different age classes showed high antioxidant activity.^[28]

Table 1: Ingredients/isolated compounds from the different parts of *Cassia fistula* plants

Plant organ	Active ingredients/isolated compounds	Reference
Stem bark	Lupeol, β -sitosterol and hexacosanol	[14]
Fruits pulp	1,8-dihydroxy-3-anthraquinone derivative	[15]
Fruit tissue	Rich source of potassium, calcium, iron, and manganese	[19]
Flowers	Kaempferol, leucopelargonidin tetramer, rhein, fistulin and triterpenes	[16]
Leaves	Anthraquinones like rhein, chrysophanol, and physcion	[21]
Leaves	Heptacosanyl-5-hydroxypentadec-2-enoate and octacosan-5, 8-diol	[18]
Seed	Galactomannan	[22]
Seeds	Seeds contains linoleic, oleic, stearic and palmitic acids and caprylic and myristic acids	[17]
Seeds	5-(2-hydroxyphenoxymethyl) furfural, (2'S)-7-hydroxy-5-hydroxymethyl-2-(2'-hydroxypropyl) chromone, benzyl 2-hydroxy-3,6-dimethoxybenzoate, and benzyl 2 β -O-D-glucopyranosyl-3,6-dimethoxybenzoate, together with other compounds, 5-hydroxymethylfurfural, (2'S)-7-hydroxy-2-(2'-hydroxypropyl)-5-methylchromone, and two oxanthraquinones, chrysophanol and chrysophanein	[20]

Finding based on albino rats was performed to check the antioxidant activities of the aqueous and methanolic extracts of the *C. fistula* Linn. bark and results confirmed that both extracts exhibited significant antioxidant activity in DPPH, Nitric oxide and Hydroxyl radical induced *in vitro* assay methods.^[9] Earlier finding showed that ethyl acetate extract showed higher antioxidant activity and order of antioxidant was noted as ethyl acetate extract > methanol extract > n-hexane extract, with antioxidant activity consecutively at 5 h with 65.98%, 58.19%, and 32.66%.^[29]

Another important study was performed to investigate the antioxidant activities of *C. fistula* with 90% ethanol extracts of leaves, and 90% methanol extracts of stem bark, pulp and flowers and its results confirmed that stem bark showed high antioxidant activity in terms of reducing power, inhibition of peroxidation, O₂⁻, and DPPH radical scavenging ability.^[30]

Previous finding examines the antioxidant activity of such as n-hexane fraction (NHF), ethyl acetate fraction (EAF), and aqueous fractions (AQF) of *C. fistula* L. pods and results revealed that antioxidant potency was high in ethyl acetate, and sequence was note as decreasing order of EAF, NHF, and AQF.^[31] Antioxidant effect of aqueous extract of *C. fistula* (Linn.) flowers was evaluated and results revealed that decreased activities of antioxidant enzymes including superoxide dismutase, catalase, glutathione peroxidase, glutathione reductase, and glutathione were reverse back to near to normal level.^[32]

Antioxidant activity of the extracts of fruit pulp was investigated and finding of the study concluded that hydroalcoholic extract of fruit pulp shows antioxidant activity via inhibiting DPPH and hydroxyl radical, total phenol content, and reducing power activities.^[33]

Anti-inflammatory activity

Inflammation is a normal physiological process in response to tissue injury, infection, and various other factors also involve in this process and cause various pathological alterations. Safe and natural remedies are needed to control the inflammatory process via modulation of pro-inflammatory cytokines and other factors involve in the chronic inflammation. Flavonoids is an ingredient present in the various medicinal plants including *C. fistula* shows role as anti-inflammatory process due to the rich source of antioxidant. It has been recognized that flavonoids show a role in the inhibition of several enzymes that are activated in the inflammatory process.^[34]

An important finding has shown that *C. fistula* Linn. bark extracts were found to possess significant anti-inflammatory effect in both acute and chronic models.^[9] The water

extract of dried fruits of *Solanum xanthocarpum* Schrad and Wendl and dried pulp of *C. fistula* Linn was prepared and anti-inflammatory activity was measured and **results revealed that** among the different dose combinations of both extracts, the 1:1 combination at the 500 mg/kg dose showed maximum percentage inhibition of 75%, which was comparable with the positive control, diclofenac sodium, which showed 81% inhibition.^[35] Another study was performed to test the anti-inflammatory effects of *C. fistula*, as compared with phenylbutazone, using carrageenin, histamine, and dextran induced paw edema in rats and anti-inflammatory activity against all phlogistic agents was noticed.^[36] Study was made to evaluate the anti-inflammatory effect of *C. fistula* with different dose of ethanolic extract of leaf (ELE) and results showed that ELE significantly inhibited both the carrageenan-induced hind paw edema and cotton-pellet granuloma in a dose-dependent manner.^[37]

Another study was carried out to evaluate the anti-inflammatory activity of aqueous and alcoholic extracts of *C. fistula* bark in sub-acute models of inflammation results confirmed that extracts showed significant anti-inflammatory effect in both air pouch granuloma and cotton pellet granuloma models.^[38]

Anti-tumor activity

Medicinal plants have an ancient history in cancer treatment via traditional medicine such Unani, Ayurveda and Chinese. Various plants and their constituents such as dates, olive, black seed have shown a role in cancer prevention via modulation of biological activities. There are many effective cancer chemotherapeutic drugs that have been derived from the natural source.^[39] An important study was performed to check the effects of methanolic extract of *C. fistula* seed on the growth of Ehrlich ascites carcinoma and on the life span of tumor bearing mice and results revealed that extract increase life span, and a decrease in the tumor volume and viable tumor cell count.^[40] A study was performed on the human colon adenocarcinoma cell line such as COLO 320 D to evaluate the anticancer activity of rhein and results revealed that rhein showed 40.59%, 58.26%, 65.40%, 77.92%, and 80.25% cytotoxicity at 200 µg/mL concentration for 6, 12, 24, 48, and 72 h incubation time.^[41] A study was carried out to evaluate the anticancer activity of different types of fruit extracts against cell lines such as human cervical cancer (SiHa) and breast cancer (MCF-7) and results revealed that seeds and pulp treated both cell lines showed up-regulation of p53 and Bax genes, down-regulation of Bcl-2 gene and increased caspase-3, 7 and 10 and-9 enzymes activities.^[42] Furthermore, rhein also showed inhibition of growth of cancer cell lines including human cervical cancer (SiHa), breast adenocarcinoma (MCF-7) and hepatocellular carcinoma (HepG2) in a dose-dependent manner.^[43]

Anti-diabetic activity

Diabetic mellitus is a metabolic disease and also a major health problem worldwide. Drugs based on allopath used to treat the diabetes and its complications but these drugs show adverse complications. Most of plants have various constituents such as glycosides, alkaloids, terpenoids, flavonoids, carotenoids that are commonly implicated as anti-diabetic activity^[44] and has a role in diabetes control since ancient time. The exact mechanism of action of medicinal plants in the management of diabetes is not understood completely, but it is considered that medicinal plants show role in the increase of the insulin-stimulated glucose uptake. A study reported that hexane extracts of *C. fistula* bark at a dose $0.15 \times 0.30 \times 0.45$ g/kg body weight for 30 days suppressed the elevated glucose levels in diabetic rats.^[45] Methanolic extract of bark and leaves at 500 mg/kg dose showed significant anti-hyperglycemic and anti-lipidemic activity than 250 mg/kg in the STZ-nicotinamide-induced DM rats^[46] and other finding result conclude that the extract and fraction evaluated for anti-diabetic activity revealed appreciable results in decreasing the serum glucose level and other complications associated with diabetes.^[47]

Other study based on the preparation of aqueous extract and synthesis of gold nanoparticles was performed to evaluate the hypoglycemic effects, and results confirm that *C. fistula* gold nanoparticles have promising antidiabetic properties.^[48] Stem barks of *Tamarindus indica* and *C. fistula* were evaluated for anti-hyperglycemic effect in alloxan-induced diabetic rats and results revealed that a significant decrease in blood glucose level in diabetic rats treated.^[49] Oral administration of catechin (20 mg/kg b.wt) for 60 days produces a better glucose tolerance pattern in Streptozotocin-induced diabetic male albino Wistar rats.^[50]

Anti-bacterial activity

Diseases related to microbes infections are one of the major causes in the morbidity and mortality worldwide especially in the developing world. Nowadays, treatment based on antibiotics is effective in diseases control but also causes drug-resistant. A range of plants and its constituents have proven pivotal role in the control of infectious diseases through the breakdown of bacterial cell wall. However, *C. fistula* shows a pivotal role in the management of infectious diseases especially due to their inhibitory effect on various types of the pathogen.

The antibacterial and antifungal activities of hydroalcohol extracts of leaves of *C. fistula* were tested against Gram-positive, Gram-negative, fungal strains, and results showed that significant inhibition of the bacterial growth was shown against the tested organisms.^[51] An important study was made to evaluate the antibacterial and antifungal activities

of extracts of *C. fistula* against Gram-positive, Gram-negative human pathogenic bacteria and fungi and crude extracts showed moderate to strong activity against most of the bacteria tested.^[52] Other finding was performed to evaluate the methanolic and ethanolic extracts of *C. fistula* against Gram-positive and Gram-negative species and both extracts efficiently inhibited three Gram-positive species including *Staphylococcus aureus*, *Staphylococcus epidermidis* and *Bacillus cereus* and two Gram-negative bacteria including *Escherichia coli* and *Klebsiella pneumonia*.^[53] A different types of extract such as hexane, chloroform, ethyl acetate, methanol, and water from the flower were evaluated against bacteria and results showed that all extracts exhibited antibacterial activity against Gram-positive organisms and in Gram-negative bacteria, only *Pseudomonas aeruginosa* was susceptible to the extracts.^[54]

Another finding reported that plant protease inhibitors like fistulin was found to be very active against *S. aureus*, *E. coli*, *B. subtilis*, and *K. Pneumonia*.^[55] and methanol extract of *C. fistula* seeds was effective on the tested microorganism and the minimum inhibitory concentration values were found in the range of 1.563–50.00 mg/ml.^[56]

Results of the study confirmed that antibacterial activity of compound 1 isolated from *C. fistula* was fairly good against Gram-negative bacteria and Gram-positive bacteria and antifungal activity of compound 1 was found to be greater against *Aspergillus niger* and *Fusarium oxysporum*.^[57]

An vital study has revealed that isoflavone biochanin A compound showed 50% effective concentration (EC (50)) value of 18.96 µg/mL against promastigotes of *Leishmania* (L.) chagasi and also showed anti-Trypanosoma-cruzi activity, resulting in an EC(50) value of 18.32 µg/mL and a 2.4-fold more effectiveness than benznidazole.^[58]

Hepatoprotective effect

Various chemicals such as high dose of paracetamol/anti-analgesic/anti-pyretic, excess alcohol consumption, infections, and toxic materials cause alterations in liver cells mainly by lipid peroxidation. In this vista, natural products have proven pivotal role in the management of liver via detoxification of toxic materials or excretion of toxic materials through urine. A study based on aqueous extract of *C. fistula* was performed and results exhibited dose-dependent reduction in total bilirubin, alkaline phosphatase, serum glutamic oxaloacetic transaminase (SGOT), serum glutamic pyruvic transaminase (SGPT), aspartate transaminase, alanine aminotransferase and increase in total protein levels and extract-treated groups show mild hepatocytic damage compared to the CCl₄ treated group.^[59] Other finding reported that pretreatment of ethanolic leaf extract of *C. fistula* (500 mg/kg body

weight/day for 7 days) followed by CCl_4 treatment totally reversed back lipid peroxidation and the activities of catalase and glutathione reductase in the liver tissue towards normal.^[60] Hepatoprotective activity of extract n-heptane of *C. fistula* leaves was evaluated and results confirmed that extract of *C. fistula* at a dose of 400 mg/kg showed significant hepatoprotective activity which was comparable to that of a standard hepatoprotective agent.^[61]

A key study was performed to evaluate the hepatoprotective activity of the n-heptane extract paracetamol-induced hepatotoxicity and results revealed that extract at a dose of 400 mg/kg body wt. showed significant protective effect via lowering the serum levels of transaminases (SGOT and SGPT), bilirubin and alkaline phosphatase.^[62] Treatment with aqueous extract of leaves and bark of *C. fistula* significantly reduced CCl_4 -induced elevation in plasma enzyme and bilirubin concentration in rats.^[63] Other finding evaluated the hepatoprotective effect via methanolic extract of *C. fistula* and results demonstrated that treatment with methanolic extract (200 mg/kg and 400 mg/kg) reversed back the altered level of biochemical markers to the near normal levels in the dose-dependent manner^[64] and a study also reported hepatoprotective effect of *C. fistula*.^[65]

Anti-pyretic effect

Cassia fistula and its constituents show role as anti-pyretic and earlier finding supported the anti-pyretic effect of *C. fistula* based on the animal model. An important study was performed on experimental rats to examine the anti-pyretic activities of ethanolic extract of *C. fistula* and results showed that extract at 250 and 500 mg/kg b.wt reduced TAB vaccine-induced pyrexia after 60 min, whereas at 750 mg/kg b.wt reduced the vaccine induced elevated body temperature post 30 min of its administration.^[37] Other study was aimed to evaluate the antipyretic activity of pod of *C. fistula* Linn and results confirmed that methanolic extract showed antipyretic activity, which was significantly higher than control rats.^[66]

Anti-infertility effect

Medicinal plant and their constituent have been reported their role in reproduction and control of hormone involve in reproduction. An important study based on animal model has shown that oral administration of extract seeds of *C. fistula* such as aqueous extract to mated female rats from day 1-5 of pregnancy at the doses of 100 and 200 mg/kg body weight resulted in 57.14% and 71.43% prevention of pregnancy, respectively, and furthermore, 100% pregnancy inhibition was noted at 500 mg/kg bw.^[5]

Immunomodulatory effect

A study has investigated the immunomodulatory effect of *C. fistula* in rats and study stated that *C. fistula* shows a

significant stimulation of the cell-mediated immunity and no effects on the humoral immunity.^[67]

Larvicidal and ovicidal activity

Mosquitoes are the main culprit in the vector-borne diseases such malaria, filariasis and encephalitis and yellow fever, and other viral diseases. The formulation such as mosquito coil and insecticides causes adverse effect on human health and shows resistance in mosquitoes. Several plants or their constituents show role as insecticides and also kill or inhibit the growth of mosquitoes and also they are safe and inexpensive. Earlier finding reported the activity of different plant extracts/oil against mosquito larvae^[68-70] and *Pelargonium citrosa*, *Cymbopogon citrates* and *Mentha piperita* showed larvicidal and inhibitory activity on growth against *Anopheles stephensi*.^[71-73]

A study was performed to test the methanolic leaf extract of *C. fistula* for larvicidal and ovicidal activity against *Culex quinquefasciatus* and *Anopheles stephensi* and finding demonstrated that extract such as leaf is promising for larvicidal and ovicidal agent against *C. quinquefasciatus* and *A. stephensi*.^[74] Other study assessed the role of larvicidal efficacy of different solvent flower extract against *Culex tritaeniorhynchus*, *Aedes albopictus* and *Anopheles subpictus* and from the results it was concluded that crude extract of flower was an excellent potential for controlling *C. tritaeniorhynchus*, *A. albopictus* and *A. subpictus* mosquito larvae.^[75]

The activity of methanol extract of leaves was evaluated against *Anopheles* mosquito and results confirmed that leaf extracts showed promising mosquitocidal efficacy against *A. stephensi*.^[76]

Wound healing effect

Numerous medicinal plants have confirmed their role as wound healing and also show a role in wound treatment. An important study results has revealed that *C. fistula* treated rats showed better wound closure, improved tissue regeneration at the wound site, and supporting histopathological parameters pertaining to wound healing.^[10] Another study was performed to examine the wound healing effect of methanol extract in the form of an ointment in two types of wound models such as excision and inclusion wound model rats and results confirmed that ointment of two different concentrations responded significantly in both models of wounds tested.^[77]

Toxicity and safe dose

Toxicity and safe dose of any plants and its ingredients are very crucial in the use of health management. Some plants show an adverse effect at certain dose but also shows therapeutic role at other dose. Therefore, dose and

toxicity should be checked before the use of any plant or products from the plants to avoid the unwanted adverse effect. Numerous studies have confirmed a safe dose of various plants based on animal model testing. The results of an important study has shown that *C. fistula* infusion when compared to senokot tablet showed that the infusion of *C. fistula* pods possessed very low levels of toxicity, with LD50 of 6600 mg/kg and furthermore, did not show any pathological effects on the organs examined microscopically^[78] and acute toxicity studies with the extracts of *T. indica* and *C. fistula* showed no signs of toxicity up to a dose level of 2000 mg/p.o.^[49] Another study reported that acute toxicity study with the extracts showed no sign of toxicity up to a dose level of 2000 mg/po.^[9]

CONCLUSION

The currently used drugs based on synthetic drugs show adverse effects and also alter the various biological pathways. Alternative medicine has opened a new window in health management due their inexpensive and fewer side effect qualities. *C. fistula* is an Indian labarum has an ancient history in Indian and Chinese systems of medicine in different diseases via anti-inflammatory, antioxidant, chemopreventive, and chemotherapeutic activity. The safety and efficacy and less side effect of *C. fistula* make it a potential candidate in treatment and prevention of various diseases. Recent studies based on *in vivo* and *in vitro* have confirmed that *C. fistula* shows a role in diseases inhibition via modulation of various physiological and biochemical process. Still exact mechanism of action in the diseases prevention is not fully understood. Detailed study based on molecular pathways should be made to confirm the exact mechanism of action of *C. fistula* in the diseases management.

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