Review of Literature
Cassia fistula Linn (*Leguminosae – Caesalpiniaeae*) is native of India and also grown in Mauritius, South Africa, Mexico, Brazil, China, Nepal, West Indies and East Africa (Chatterjee and Pakrashi, 1992; Trease and Evans, 1985). It is grown as an ornamental plant due to its beautiful bunches of yellow flowers (Allen and Allen, 1981; Bahorun *et al*., 2005). *C. fistula* probably originates from India and Sri Lanka, but is now pan tropical. *Cassia fistula* has been extensively used in the folklore medicine for the treatment of a variety of disease. In Indian literature there are multiple descriptions regarding its usefulness in the treatment of various diseases. Many authors have reported its antibacterial, antioxidants, hepatoprotective and hypoglycemic potentials (Perumal *et al*., 1998; Kashiwada *et al*., 1990; Bhakta *et al*., 1999; Das *et al*., 2008; Malpani *et al*., 2010). Some authors have indicated towards the free radical scavenging and antioxidant potential of *C. fistula* both in *vitro* as well as *in vivo* (Rizvi *et al*., 2009; Chaminda *et al*., 2001; Luximon-Ramma *et al*., 2002; Kannampalli *et al*., 2005). At present 600 species of genus *Cassia* have been reported (Panda *et al*., 2009; Omoregie *et al*., 2010). Treatment of various ailments in ancient India, dating back to *Surshruta Samhita* and *Charaka Samhita* (Nandkarni 1954; Rizvi *et al*., 2009) have been reported. In Ayurvedic medicinal system, *Cassia fistula* is used against pruritus, leucoderma, diabetes and haematemesis and various ailments (Satyavati and Sharma, 1989; Alam *et al*., 1990; Aslolkar *et al*., 1992). It is one of the ingredients of the preparation known as *Constivac* (Lupin Herbal) a bowel regulator which relieves constipation. It is also one of the ingredient of the preparation known as *Pilex, Purian* (Himalaya Drug Company) for piles and detoxifier respectively (Danish *et al*., 2011). The genus *Cassia* has other species like *C. tora, C. occidentalis, C. hirsute, C. auriculata, C. fruticosa, C. alata, C.sophera, C. javanica, C. ligustrina, C. singueana, C. absus, C. nodosa, C. nigricans, C. rodbughii* (Hutchinson and
Dalziel, 1958). These species have also been described to have medicinal and local uses by traditional healers (Elujoba et al., 1999; Abo et al., 2000; Ayo, 2010).

Ayurveda recognizes the *Cassia fistula* plant as Aragvadha, meaning “disease killer”.

**Sramsana**- Amaltas expels the aggravated doshas out of the body.

**Jwaranuta**- It is useful in management of any type of fever.

**Hrudaroganuta**- It manages all types of discomforts in the heart region.

**Mridu Virechana**- It reduces soft purgation. (MMPND, 2005).

### 2.1 Synonyms

<table>
<thead>
<tr>
<th>Language</th>
<th>Synonym</th>
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<tr>
<td>Hindi</td>
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<tr>
<td>Sanskrit</td>
<td>Aragvadha (disease killer)</td>
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<tr>
<td>English</td>
<td>Golden Shower, Indian Labrum, Golden Shower, Purging Cassia, Canafistula Laburum</td>
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<td>Soondali, Sonlu</td>
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<td>Kannad</td>
<td>Kakkemara (Ayurvedic pharmacopoeia, 2007)</td>
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### 2.2 Classification

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<tr>
<td>Species</td>
<td><em>fistula</em></td>
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</table>
2.3 Description of *Cassia fistula* plant

*C. fistula* is a medium-sized tree growing to 10-20 m tall with fast growth.

**Leaves**

Alternate, petiolate, leaflets ovate. The leaves are deciduous or semi-evergreen 15-60 cm long, pinnate with 3-8 pairs of leaflets. Each leaflet is 7-21 cm long & 4-9 cm broad.

**Flowers**

Bracteate, ebracteate, zygomorphic, bisexual and hypogynous. The flowers are produced in pendulous racemes. 20 - 40 cm long, each flower 4 - 7 cm diameter with five yellow petals of equal size and shape. Sepals 5, polysepalous, yellowish green in colour. Petals 5, polypetalous, stamens 10, arranged in two whorls of five each, anthers dorsfixed, ovary superior.

**Fruit and seed**

The fruit is legume, 30-60 cm long and 1.5-2.5 cm broad, with a pungent order and containing several seeds, seeds lenticular, light brown lustrous (Orwa et al., 2009).

2.4 Phytochemicals in different parts of *C. fistula*

Phytochemicals are chemical compounds formed in the plants during normal metabolic processes. These chemicals are often referred to as secondary metabolites. There are several classes including alkaloids, flavonoids, coumarins, glycosides, gums, polysaccharides, phenols, tannins, and terpenoids (Harbone, 1973; Okwu, 2004). Phytochemicals are non-nutritive plant chemicals that have protective or disease preventive properties. The different qualitative chemical tests were carried out the different plant extracts using standard procedures to identify the phytochemicals as described by sofawara (1993); Trease and Evans (1989); Harborne (1973) and Edeoga et al., (2005).
Fruit

The pulp contains sugar, tannic matter, albuminus starch, oxalate of calcium and other constituent (Gupta, 2010; Chopra et al., 2006). Modi and Khorana (1952) have identified a major anthraquinone derivative ‘rhein’ in the pulp. They have also been confirmed the compound 1, 3-dihydroxy-3-anthraquinone carboxylic acid from the pods. Kapadia and Khorana, (1966) has revealed that free rhein are complexed with sennidin like compounds in C. fistula pods. A new colouring matter fistulic acid, an anthraquinone acid has been reported from the pods (Agarwal et al., 1972). Vasi and Kalintha, (1980) estimated the 19.94% protein and 26.30% carbohydrate contents in the fruit and indicated as an important source of nutrients and energy.

The edible fruit tissue of the C. fistula fruit has been reported to be a rich source of potassium, calcium, Iron, and manganese (Barthakur et al., 1995). They have also been reported 15.3, 13 and 7.8% of aspartic acid, glutamic acid and lysine of the total amino acids respectively in the pulp. Misra et al. (1996) isolated apolar compounds including 5-nonatetracontanone, 2-hentriacontanone, triacontane, 16-hentriacontanol and sitosterol along with an oil (an isoprenoid compound) from the pod of C. fistula. It showed antibacterial activity. An anthraquinone derivative, characterized as 3-formyl-1-hydroxy-8-methoxy-anthraquinone was isolated from the pods (Rani and Kalidhar, 1998). Luximon-Ramma et al. (2002) have studied that pod contained the highest level of phenolic compound.

Leaves

Leaves contain anthraquinone, oxyanthraquinone, tannin, rhein and volatile oils (Gupta, 2010; Chopra et al., 2006). Kaji et al. (1968) have reported free rhein, rhein glucoside and sennosides A and B in leaves. Morimoto et al., (1988) have isolated (−) -epiafzelechin 3-O-B-D glucophranoside, 7 biflavanoids and two triflavanoids together with (−) epiafzelechin, (−) epicatechin and procyanidin B-2 from the leaves. Mahesh et al. (1984), Khanna & Chandra, (1996) have studied the anthraquinones chrysophanol, rhein and physcion in the leaves. The characterization of
sennosides and their contents in leaves have been reported by many Scientists (Lohar et al., 1975; Asseleih et al., 1990; Chowdhury et al., 1996).

Luximon-Ramma et al. (2002) have showed that young and old leaves contain highest total phenolic flavonoid and proanthocyanadin contents. Evaluation of phytochemicals such as alkaloids, flavonoids, carbohydrates, glycosides, protein and aminoacids, saponins and triterpenoids have been revealed the presence of most of constituents in polar extracts compared with non polar extracts (Panda et al., 2011).

Seed

Sen and Shukla (1968), Niranjan and Katiyar (1979) have noted a percentage of 31% of crude proteins comprising mainly globulin and albumin in the wild seed. They have also found that seeds were rich sources of cephalin and lecithin phospholipids and have contained 11.8% carbohydrates. One of the major carbohydrate galactomannan is reported by Lal and Gupta, 1976. Abu sayeed et al. (1999) revealed that seeds were rich in glycerides with linoleic, oleic stearic and palmitic acids together with traces of caprylic and myristic acids. Kuo et al., (2002) have identified four new compounds, 5-(2-hydroxy phenoxymethyl) furfural (1), (2’S)-7 - hydroxy - 5 – hydroxyl methyl - 2- (2'-hydroxy propyl) chromone (2), benzyl 2-hydroxy-3, 6-dimethoxybenzoate (3) and benzyl 2 beta-O-D-glucopyranosyl-3, 6-dimethoxy benzoate (4). Four other known compounds, 5-hydroxy methyl furfural, (2’S) -7- hydroxyl - 2- (2'-hydroxy propyl) - 5-methyl chromone and two oxyan thraquinones, chrysophanol and chrysophanein have also been isolated and identified in same experiment from the seeds of C. fistula.

Yadav and Verma (2003) have isolated a new bioactive flavone glycoside 5,3',4'-tri-hydroxy-6-methoxy-7-O-alpha-L-rhamnopyranosyl-(1->2)-O-beta-D-galactopyranoside with antimicrobial activity from acetone soluble fraction of the defatted seed of C. fistula.
Review of Literature

Flowers

Bhalodia et al. (2011) have found that flowers of *C. fistula* have been contained tannins, flavoniods, saponins, steroids, glycosides protein and aminoacids in higher amount. Kumar et al. (1966) have isolated a bianthraquninone glycoside, fistulin, together with Kaempferol and rhein from ethanol extracts of *C. fistula* flower. Narayanan and Seshadri (1972) have reported the presence of kaempferol and a proanthacyanidin tetramer having a free glycol in the acetone extract of flowers. Asseleih et al. (1990) have studied a certain amount of alkaloids in the flowers. Traces of triterpenes have been observed in flowers, (Gurib-Fakim et al., 1994). Mondal et al. have (1998) identified free aminoacids such as phenylalanine, methionine, glutamic acid and proline. Aurantiamide acetate (0.011), β sitosterol (0.006) and its β D glucoside (0.02%) have been isolated from flowers (Rastogi and Mehrotra, 2004).

Roots

The roots of *C. fistula* have been reported as tonic, astringent, febrifuge and purgative due to its phytochemical constituents (Gupta et al., 2008; Agrawal and Paridhavi 2005). Vaishnav and Gupta (1996) have showed the presence of rhamnetin 3-0-gentibioside in *C. fistula* roots. Root bark besides tannins contains phlobaphenes and oxyanthraquinone substances (Chopra et al., 2006; Agrawal and Paridhavi 2005). 7-methylphyscion, betulinic acid and β sitosteral have been isolated from the roots (Vaishnava et al., 1993; Rastogi and Mehrotra 2004).

Other Parts

Padmanabha Rao and Venkateswarlu (1965) have extracted fistucacidin, an optically inactive leucoanthocyaindin (3, 4, 7, 8, 4-pentahydroxyflavan) from the heart wood. The stembarks have been shown to contain lupeol, beta sitosterol and hexacotanal (Gupta et al., 1989). Rani et al. (1998) have shown the presence of oxyantrroquinone and dihydroxyanthro- quinone from bark. Luximan – Ramma et al. (2002) have
observed proanthocyanidin and flavonoid in vegetative and reproductive organs of *C. fistula*.

Priya *et al*. (2010) have isolated an anthraquinonen derivative, 6-9 dimethyl-3-methyl,1,4,5-trihydroxy-anthraquinone-2-carboxylic acid from the root of *C. fistula*. It is an antifungal constituent.

### 2.5 Phytochemical evaluation of the plant extract

Many scientists have confirmed the presence of alkaloids, glycosides, tannins, phenolic compounds, carbohydrates, steroids and terpenoids in the different extracts of different parts of *C. fistula* using qualitative chemical tests (Singh and saxena, 2011; Panda *et al*., 2010; Bhalodia *et al*., 2011; Veerachari *et al*., 2011)

**Thin layer chromatography (TLC)**

Thin layer chromatography (TLC) is a chromatography technique used to separate mixtures (Harwood *et al*., 1999). It is the simplest and cheapest method to detect plant constituents because the method is easy to run, reproducible and requires little equipment (Marston *et al*., 1997). Thin layer chromatography is performed on a sheet of glass, plastic, or aluminum foil, which is coated with a thin layer of adsorbent material, usually silica gel, aluminium oxide, or cellulose. This layer of adsorbent is known as the stationary phase. After the sample has been applied on the plate, a solvent or solvent mixture (known as the mobile phase) is drawn up the plate via capillary action. Because different analytes ascend the TLC plate at different rates, separation is achieved (Vogel *et al*., 1978). However, some disadvantages of this method are that it lacks good baseline separation, validation, sensitivity limits and takes a longer analysis time.

**High performance liquid chromatography (HPLC)**

It is basically a highly improved form of column chromatography. Instead of a solvent being allowed to drip through a column under gravity, it is forced under high pressures. This allows a much better separation of the
components of the mixture. There are two variants of HPLC depending on the relative polarity of the solvent and the stationary phase.

**Normal phase HPLC**

The column is filled with tiny silica particles, and the solvent is non-polar. Polar compounds in the mixture being passed through the column will stick longer to the polar silica than non-polar compounds. The non-polar ones will therefore pass more quickly through the column.

**Reversed phase HPLC**

In reversed phase HPLC, the silica is modified to make it non-polar by attaching long hydrocarbon chains to its surface. A polar solvent is used. For example, a mixture of water and an alcohol such as methanol. In this case, there will be a strong attraction between the polar solvent and polar molecules in the mixture being passed through the column. There won’t be as much attraction between the hydrocarbon chains attached to the silica (the stationary phase) and the polar molecules in the solution. Polar molecules in the mixture will therefore spend most of their time moving with the solvent. Non-polar compounds in the mixture will tend to form attractions with the hydrocarbon groups because of vander waals dispersion forces. This means it is the polar molecules that will travel through the column more quickly. Reversed phase HPLC is the most commonly used form of HPLC (Pranav kumar, 2010)

2.6  **Medicinal properties of C. fistula**

2.6.1  **Laxative Properties**

Both the leaves and pods are widely used in traditional medicines as strong laxatives and purgative suitable for children and pregnant women (Satyawati and Sharma, 1989; Van, 1976) and have also been reported to treat intestinal disorders like healing ulcers (Biswas et al., 1973; Kirtikar and Basu, 1975). *C. fistula* is widely used for its medicinal properties, its main property being that of mild laxative and is also a purgative due to the wax aloin and a tonic due to present of sennoside and rehin. Akanmu et al.,
(2004) have concluded that *C. fistula* pod infusion could safely be utilized as laxative drug and substitute for the *Official senna*.

The contents of anthraquinone glycoside in the leaves and decoction leaf extracts of *C. fistula* will be useful for finding a good source of alternative herbal laxative drugs and promoting standardization of plant raw material and its extract. The central and north-east dried leaf sample contains about 0.5% w/w of total anthraquinone glycosides. Thus they have the ability to be developed as an alternative herbal laxative drug and used instead of *C. fistula* pods (Sakulpanich *et al.*, 2009).

**2.6.2 Antibacterial properties**

Patel and Patel (1956) have studied the antibacterial potential of alcohol and aqueous extracts of *C. fistula* fruit and seed and have observed that the dealcoholized extract of the pulp shows greater effect on gram-positive bacteria than aqueous extract. While in the case of gram negative bacteria both kind of extracts exhibit a similar effect.

Perumal *et al.* (1998) have tested antibacterial activity of aqueous, diethyl ether, ethyl acetate dichloromethane and methanol extract of *C. fistula* leaves against *E. coli*, *Klebsella aerogenes*, *Protious vulgaris* and *Pseudomonas aerogense* at 1000 – 5000 ppm using the disc diffusion method. They have found significant inhibitory effect against all microorganisms.

Abbas *et al.* (2004) have purified three lectins CSL-1, CLS-2 and CSL-3 from *C. fistula* seeds and tested for antibacterial activities against fourteen pathogenic bacteria using 30µg/disc. The lectin CLS-3 has been found to be active against all of the bacterial strains and has shown strong activity against *Bacillus megateerium*, *Streptococcus β-haemolyticus* and *Shigella boydii*. The lectin CSL-2 shows poor activity against most of the bacterial strains and has strong activity against only *streptococcus β haemolyticus*. While the lectin CSL-1 has been found to be inactive against all bacterial strains except *Streptococcus β haemolyticus* and *Sarcina lutea*. 
Yogesh and Mohan (2006) have observed that methanol extract of *C. fistula* linn is found to be more effective against *Salmonella paratyphi* and *S. aureus*. Kumar *et al.* (2006) have studied that dichloromethane and methanol extracts were effective against *Bacillus cereus, Bacillus pumilus, Bordecella bronchiseptica, Microoccus, S. aureus, S. epidermidis, E. coli and Klelebsiella pneumoniae*.

Duraipandiyan and Ignacimuthu (2007) have reported antibacterial potential of hexane, chloroform, ethyl acetate, methanol and water extracts of flower of *C. fistula* against Gram positive organisms with MIC between 0.078 and 2.5 mg/ml. Among the gram negative bacteria only *Pseudomonas aeruginosa* is susceptible to the extracts.

Ali *et al.* (2007) have used amoxicillin in combination with water extract of fruit of *C. fistula*, as Amoxy-Cassia. They have successfully formulated new, cost effective antimicrobial combination for Multi Drug Resistant (ADR) *Salmonella enterica, Serover Typhi* (SETS) based on the synergistic activity of amoxicillin with *C. fistula*.

Sangetha *et al.* (2008) have reported that methanolic extracts prepared from different parts of *C. fistula* have antibacterial effect against *S. typhi, E. coli, Azospirillum lipoferum, K. pneumoniae, S. aureus, P. aerogenes and B. subtilis*.

Vimalraj *et al.* (2009) have tested antibacterial activity of aqueous and alcoholic extract of stem bark against pathogenic bacteria of veterinary importance. They have observed activity only against *S. aureus*. The zone of inhibition for *Staphylococcus aureus* to alcoholic and aqueous extracts are in the range of 7.0 – 12 mm and 7.0 – 11.6 mm.

Vasudevan *et al.* (2009) have shown that alcoholic extract of leaves of *C. fistula* have significant antimicrobial activity against *S. aureus, P. aeruginosa, E. coli and Group A Streptococci*. They observed that the aqueous extract is liquid-liquid partition between chloroform-methanol in 1:1
and 2:1 which shows the highest antimicrobial activity against *S. aureus*, *P. aeruginosa*, *E. coli* and Group A *Streptococci*. In the same study the biossay guided isolated compounds have shown minimum bacterial concentration (MBC) values ranging from 4 mg/ml – 8mg/ml and MIC values ranging from 1 mg/ml – 2 mg/ml.

Awal *et al.* (2010) have studied *in-vitro* antibacterial activity of ethanol extracts of leaf and roots of *C. fistula*. They have found that the leaf extract showed comparatively better antibacterial property at concentration of 30 µg/disc against five gram positive namely *Sarcina lutea*, *Bacillus megaterium*, *Bacillus subtilis*, *Streptococcus β-haemolyticus*, *Staphylococcus aureus* and nine gram negative bacteria – *Salmonella typhi*, *Shigella dysenteri*, *Shigella boydii*, *Shigella sonnei*, *Shigella flexneri*, *Shigella shaaga*, *E. coli*, *Pseudomonas aeruginosa* and *Klebsiella pneumoniae*. While ethanolic extract of root shows lower sensitivity.

Venkatesan and Karrunakaran *et al.* (2010) have observed that alcoholic extract of aerial parts of *C. fistula* show activity against *S. aureus and E. coli*.

Growther & Janardhanan (2010) have found that ethanol, methanol and petroleum ether extract of *C. fistula* exhibit antibacterial effect against MRSA (Methicillin resistant *Staphylococcus aureus*) and MSSA (Methicillin sensitive *Staphylococcus aureus*).

Bhalodia *et al.* (2011) have evaluated the antibacterial potential of hydroalcohol and chloroform extract of flowers of *C. fistula*. They have found that the extracts are effective against *Staphylococcus aureus*, *Streptococcus pyogenes*, *E. coli* and *P. aeruginosa* and have found the dose dependant antibacterial activity.

Singh and Jain (2011) have studied the antibacterial properties of alcoholic extract of flower materials of *C. fistula*. They have observed that the extracts exhibit activity against *B subtilis*, *K. pneumonia*, *Pseudomonas aeruginosa* and *S. aureus*. 
Aneza et al. (2011) have reported that the organic flower and bark extract of C. fistula exhibit the antibacterial activity against S. aureus, P. minlabilis, E. coli, P. aeruginosa, Acinetobacter sp. and C. albicans, ear pathogens causing otitis externa. While organic leaves extracts do not exhibit any activity against P. aeruginosa and C. albicans. S. aureus has been found to be the most sensitive pathogen having an MIC of 6.25 mg/ml. Other tested pathogens were found to be less sensitive, having MIC values between 25 mg/ml and 50 mg/ml.

2.6.3 Antifungal Activity

Farnsworth and Bunyapraphatsara (1992) have studied the antifungal activity of C. fistula and other species of Cassia. C. alata and C. tora which are recommended for primary health care in Thailand to treat ringworm and other fungal diseases. This plant has been widely used by tribal people to treat various ailments including ringworm and other fungal skin infections (Rajan et al., 2001). Phongpaichit et al. (2004) have investigated that C. fistula has been the most potent inhibitor of P. marneffei and methanol extracts of C. alata, C. fistula and C. tora inhibit the hypal growth of Trichophyton rubrum, Penicillium marneffli and Microsperum gypseum. Dichloromethanolic and methanolic extract of pod of C.fistula exhibit activity against Aspergillus niger (Kumar et al., 2006)

Sharma et al. (2006) have studied the antifungal property of crude as well as partially purified fractions of C. fistula pulp and have observed that the inhibitory activity on the fungus A. niger. They have further observed that secondary metabolites present in the extract were possibly responsible for the inhibition of fungus.

Singh and Karnwal have (2006) evaluated the antifungal activity of acetone diethyl ether and methanol extract of leaves of C. fistula and have observed that the methanol extract exhibits highest activity (21 mm) for C. albicans.
A crystal has been isolated, which has been confirmed as 4-hydroxy benzoic acid hydrate from the flower of *C. fistula*. This compound exhibits antifungal activity against *Trichophyton mentagrophytes* and *Epidermophyton floccosum* (MIC 0.5 mg/ml) (Drudiphandiyan and Ignacimuthu, 2007).

Methanolic extracts prepared from different parts (leaves, flowers, stem and pods) of *C. fistula* have been evaluated for antimicrobial activity against medically important bacterial, yeast and fungal strains. These extracts have been reported effective against *Micrococcus sp.*, *S. typhi*, *E. coli*, *Azospirillum lipoferum*, *K. pneumoniae*, *S. aureus*, *E. aerogenes*, *B. subtilis* (Sangetha et al., 2008).

Panda *et al.* (2010) have been evaluated antifungal activity of petroleum ether, chloroform, ethanol, methanol and aqueous extracts of *C. fistula* leaves. They found that all extracts exhibit antifungal activity against *Candila albicans* (12.6 mm), *C. krusei* (13.3 mm), *C. parapsilosis* (14 mm) and *C. tropicalis* (14.3 mm). Petroleum ether and ethanol extracts have also shown the zone of inhibition for *A. niger* (12.0 mm).

Priya *et al.* (2010) have found that methanol extract of bark showed good antifungal activity than other extracts of different parts due to presence of antifungal constituent anthraquinone derivative.

Bhalodia *et al.* (2011) have tested antifungal activity of hydroalcohol and chloroform extracts of flowers and have found that both the extracts are effective against *Aspergillus niger*, *A. clavatus*, and *C. albicans*.

### 2.6.4 Antiviral Activity

Ethanolic extract of pod and stem bark of *C. fistula* have been to be active against Ranikhet disease virus (RDV) and *Vaccinia* virus (Dhar *et al.*, 1968). Some other species of *Cassia* also have been reported to have antiviral activity. Hussein *et al.* (2006) have reported that the *Cassia obtusifolia* have activity against HIV-1. Cheng *et al.* (2006) have observed
that *C. javanica* inhibits herpes simplex virus (HSV-2). Narong *et al.* (2007) have found that *C. fistula* fruit has activity against foot and mouth disease virus (FMD virus).

### 2.6.5 Antiparasitic Activity

Sartorelli *et al.* (2007) have showed antilashmanial activity against the promasfigote forum of *Hushmania Changasi*. They have presented 50% inhibitory concentration (IC$_{50}$=10.03 µg/ml) and intracellular amenstigotes demonstrated IC$_{50}$ value of 18.10 µg/ml. In the same experiment Clerosterol compound has been isolated from the fruit of *C. fistula*, which infer IC$_{50}$ of 10.03µg/ml for intracellular amastigotes and recommended as antileishmanial compound.

In another study Sartorelli *et al.* (2009) have isolated biochanin-A an isoflavone compound from dichloromethane extract of fruits of *C. fistula* which infer 50% effective concentration value of this compound 18.96 µg/ml against promastigot of *Leishmania chagasi*. They have also studied that biochanin-A showed anti *Tripanosama-cruzi* activity with effective concentration value of 18.32 µg/ml.

Jaffary *et al.* (2010) have evaluated the potential of *C. fistula* boiled extract in the treatment of cutaneous leishmaniasis. They have observed efficacy of intraleisional meglumine antimonite and *C. fistula* fruit gel combination for the treatment of cutaneous leishmaniasis. A total of 140 patients with cutaneous leishmaniasis in which, one group received intraleisional meglumine antimonite injection and *C. fistula* fruit gel, and the second group (control) was treated with intraleisional meglumine antimonatge plus placebo gel. At week 12, forty-seven (67.1%) patients in the experimental group achieved complete cure compared to 29 (41.4%) patients in the control group (P<0.001).
2.6.6 Antioxidant activity of *C. fistula*

Natural antioxidants play a key role in health maintenance and prevention of chronic and degenerated diseases. The antioxidant properties of different extracts of *C. fistula* have been reported both in *vitro* and in *vivo*.

Jawahar and Gupta (1972) have reported that the stem bark and leaf extracts exhibit highest superoxide radical scavenging and reducing power than other parts in a dose-dependent manner, this may be due to presence of fistucacidin present in the stem bark. It contacts a 4 ortho position hydroxyl which provides active hydrogen to take part in reaction to scavenge $O_2$.

Gupta *et al.* (1990) have shown that some of the bioactive compounds such as xanthones flavonols and proanthocyanidins present in the stem bark and leaf extract, should perform as good singlet oxygen quenchers. Kashiwada *et al.* (1990) have also noted DPPH (1,1-diphenyl-2-picrylhydrazyl-2-picrylhydrazyl) radical scavenging ability of the stem bark and leaves extract might be due to the presence of high concentration of tannins. Proanthocynidins flavonols and xanthones indicate the ability of *C. fistula* extract to act as radical scavenger and metal quencher thereby, protecting free radical mediated damage.

Sunil and Muller (1998) have reported that the methanolic extract of fruit inhibits 2, 2-azo-bis(2-amidinopropane)-dihydrochloride (AAPH) induced lipid peroxidation in bovine brain phospholipids in a concentration dependent manner. They have also observed that it inhibits the 5-lipoxygenase mediated peroxidation of arachidonic acid; free radical induced lipid peroxidation and hence inhibits leukotrienes biosynthesis.

Chaminda *et al.* (2001) have reported that the *in vitro* 1,1-diphenyl-2-picrylhydrazyl-2-picrylhydrazyl (DPPH) radical scavenging and deoxyribose damage protection properties by using aqueous extract of root. They have showed 50% effective concentration ($EC_{50}$) of $59 \pm 2.7$ $\mu$g/ml and 30% protection against deoxyribose damage at a concentration of 125$\mu$g/ml.
Sidduraju et al. (2002) have calculated DPPH radical scavenging activities in order of stem bark 93%, leaves 74.9%, butylated hydroxytoluene BHT 37.8%, flowers 33.2%, pulp 15.7% and have noted that it was directly proportional to the total phenolic content in its extract. They have also recorded antioxidant activity of methanolic and ethanoic extract of different parts of the plant in order to stem bark > leaves > flower > pulp. The stem bark extract also exhibits greater peroxidation inhibiting activity on linolic peroxidation system and liposome peroxidation system.

Suresh et al. (2008) have also reported lipid peroxidation inhibition of leaves extract.

Luximon – Ramma et al. (2002) have found highest antioxidant properties in reproductive organs of *C. fistula* in comparison to vegetative part. The antioxidant properties are in the order of pod > flower > stem > bark > leaves and it is also directly proportional to the content of total phenols, proanthocyanidins and flavanoids in extract. They have also shown that pod has the highest antioxidant potential with a TEAC value of 992 ± 0.4 and FRAP value of 811 ± 23 µg/ml dry wt. and correlation coefficient between total phenols and antioxidant capacity is 0.989 for TEAC and 0.951 for FRAP.

Raju et al. (2005) have studied the bark extract of *C. fistula* have radical scavenging capacity by inhibiting lipid peroxidation in CCl₄ and FeSO₄ induced liver homogenate.

Bhalodia et al. (2011) have observed that the hydroalcoholic extract of *C. fistula* has showed antioxidant activity of inhibiting DPPH and hydroxyl radical. Total phenol content and reducing power activities have confirmed that the hydrochloric extract of *C. fistula* could be used as source of natural antioxidants and as a possible food supplement or in pharmaceutical industry.
2.6.7 Hepatoprotective Activity

Bhakta et al. (1999) have investigated that the hepatoprotective activity of the n-heptane extract of *C. fistula* leaves in rats by inducing hepatotoxicity with carbon tetrachloride liquid paraffin (1:1). They have demonstrated that the CCl₄ liquid paraffin in rats could be elevated by treatment of n-heptane extract of *C. fistula* leaves. They have further noticed that the lowering of serum levels of transaminases (SGOT and SGPT), bilirubin and alkaline phosphate (ALP). The extract of *C. fistula* at a dose of 400µg/ml has been shown significant hepatoprotective activity which is comparable to that of a standard hepatoprotective agent.

Kannampali et al. (2005) have showed hepatoprotective activity of ethyl extracts of leaves in CCl₄ induced hepatotoxicity in rats. They have found that the oral administrations of extract restored three fold elevated malondialdehyde (MDA) level, in 30 days. The levels of superoxide dismutase and catalase, mutually supportive antioxidant enzymes, are found to be maintained by phytochemicals of *C. fistula*. Kannampali et al. (2007) have again investigated that the oral administration of ethyl extract of leaves have restored the normal values of aspartate, alanine transaminase, alkaline phosphatase, γ-glutamyl transferase, lactate dehydrogenase and serum bilirubin of serum in diethylenitrosamine (DEN) induced hepatic damage in rats.

Das et al. (2008) have evaluated hepatoprotective activity of aqueous extract of fruit pulp of *C. fistula* against the CCl₄ induced liver damage in albino rats and have showed significant activity. They have also reported that the histological structure of liver regain to near normal with congestion and regeneration of liver tissue.

Patwardhan et al. (2009) have investigated heptoprotective activity of ethanolic extract of *C. fistula* bark against hepatotoxicity induced by administering CCl₄ with olive oil (1:1). They have noticed that the hepatoprotective effect of ethanolic extract of *C. fistula* bark is evident in the
doses of 200 and 400 mg/Kg as there is a significant decrease in AST, ALT, ALP, tryglycerides, bilirubin and protein levels in comparison to CCl$_4$ control group. Histology of the liver section of the animals treated with the ethanolic extract of C. fistula bark shows no abnormality in the doses of 200 and 400 mg/Kg, further confirm the hepatoprotective activity.

Wasu and Mully (2009) have reported that aqueous extract of the C. fistula leaves and barks have been effective in the treatment of CCl$_4$ induced hepatic cytotoxicity. They have observed that the daily oral consumption of an aqueous extract of the C. fistula leaves and bark reduced the CCl$_4$ toxicity.

Chaudhari et al. (2009) have evaluated the hepatoprotective activity of the methanolic extract of C. fistula seeds by using paracetamol-induced hepatic injury in rats. They have observed that the methanolic extract reveal marked reduction in the elevated level of SGOT, SGPT, SALP and serum billurubin. It has been also noted that aqueous extract has reduced the elevated levels of SGOT, SGPT, SALP and serum billurubin to lesser extent in respect to methanolic extract.

Jahangir et al. (2010) have observed that the treatment of C. fistula leaf extract prevent INH and RIF (Isoniazd and Rifampicin) induced hepatotoxicity in rats. The higher dose of C. fistula leaf extract, have showed better results as compared to lower dose, both biochemically and morphologically. They have also noticed that the overall hepatoprotective effect of C. fistula was probably due to a counteraction of free radicals by its flavonoids acting as antioxidant.

2.6.8 Anti-inflammatory action

Raju et al. (2005) have showed that the oral administration of aqueous and methanol extract of stem bark have reduced the weight of cotton pellet granuloma and paw oedima in rats at significant level.
The anti-inflammatory activities of aqueous and alcoholic extracts of *C. fistula* bark have been studied by Rajeswari *et al.* (2006) in sub acute models of inflammation in male albino rats. They have observed that both the extracts have possessed anti-inflammatory effect in both air pouch granuloma and cotton pallet granuloma models and reduce biomarker enzymes, acid phosphates in serum.

Anwikar *et al.* (2010) have investigated anti-inflammatory activity of aqueous extract of dried fruit of *C. fistula* using the carrageenan-induced paw edema model in rats. It has been observed that extracts of dried fruit have showed maximum anti-inflammatory activity at 500 mg/Kg dose.

Gobianand *et al.* (2010) have tested the anti-inflammatory and antipyretic activities of ethanolic extract of *C. fistula* in rats and have observed dose dependent effect. Anti-inflammatory activity has been evaluated using carrageenan induced rat paw edema and cotton pellet granuloma models. The antipyretic effect has been evaluated using against TAB vaccine induced pyrexia. It has been noticed that ethanolic extract of *C. fistula* significantly inhibit both the carrageenan induced hind paw edema and cotton-pellet granuloma. Ethanolic extract at 250 and 500 mg Kg$^{-1}$ wt have reduced TAB vaccine induced pyrexia in rats after 60 minutes, whereas at 750 mg Kg$^{-1}$ wt have reduced the vaccine induced elevated body temperature post 30 minutes of its administration.

2.6.9 Analgesic and antipyretic potential of *C. fistula*

Patel *et al.* (1965) and Mazumdar *et al.* (1998) have reported analgesic and antipyretic activities of *C. fistula* seeds.

Patel *et al.* (2010) have reported that the petroleum ether, ethyl acetate, chloroform, methanol extracts of *C. fistula* bark possess a significant antipyretic effect. It has been also observed in the same study that methanol extract of bark at a dose of 300 mg/Kg body weight shows maximum antipyretic activity amongst other extracts. It is statistically significant as a the value of $p < 0.05$. 


Sheikh et al. (2010) have studied analgesic activity of *C. fistula* methyl alcohol extract (CF-MA) using hot plate method and tail clip method. They have observed that the administration of extract by intra peritoneal route at dose of 250 mg/Kg and 500 mg/Kg to wistar albino rats shows significant inhibition in pain response induced by thermal, mechanical and writhing stimuli in dose dependant manner.

### 2.6.10 Wound healing property

The ethanolic extracts of leaves have been found to have wound healing activity by tissue regeneration at the site of wound (Bhakta et al., 1998b; Muthusamy et al., 2006).

Senthil et al. (2006) have observed that *C. fistula* treated rats exhibits better wound healing, improved tissue regeneration at the wound site and supporting histopathological parameters pertaining to wound healing.

### 2.6.11 Hypoglycemic and hypocholesterolasmic activity of *C. fistula*

Singh and Bhardwaj (1975) have preliminary examined hypoglycemic effect of seed in normal rat. Esposito et al. (1991) have showed that aqueous extract of leaves significantly decrease glycemia.

Bhakta et al. (1997) have reported that the oral administration of methanol extract of leaves significantly reduced blood glucose level up to 25.2% and 45.7% at the dose of 400mg/Kg and 600mg/Kg respectively in alloxan diabetic rats. The LD$_{50}$ of the extract has been found to be 3.5g/Kg and it reduce blood glucose concentration within two hours and effect is maintained up to ten hours.

Nirmala et al. (2008) have studied that the hexane extract of *C. fistula* bark at doses 0.15, 0.30; 0.45 Kg$^{-1}$ weight for 30 days suppress the elevated blood glucose levels in diabetic rats.

Malpani et al. (2010) have studied that the ethyl acetate fraction of total alcoholic extract of the bark of *C. fistula* at the dose of 200 mg/Kg body
weight shows significant anti diabetic activity in alloxan induced diabetic rats. The ethyl acetate fraction exhibits significant reduction in blood glucose levels than alcoholic extract and have found effective in restoring blood lipids to normal levels.

El-Saadany et al. (1991) have studied that the administration of *C. fistula* significantly reduce blood and liver total lipids, blood, liver, kidney, spleen and heart total cholesterol has been significantly reduced in hypercholesterolaemic male albino rats.

### 2.7 Other bioefficacies of *C. fistula*

Bhakta et al. (1998a) have studied the antitussive activity of *C. fistula* leaf extract on a cough model induced by sulphur oxide gas in mice and have observed significant antitussive activity when compare with control. They have further revealed dose dependent effect of the *C. fistula* extract (400, 600 mg/Kg, body weight) shows maximum inhibition of cough by 44.44% and 51.85% with respect to control group.

Gupta et al. (2000) have studied the effect of methanolic extract (ME) of *C. fistula* seeds on the growth of Ehrlich ascites carcinoma (EAC) and on the life span of tumor bearing mice. In this study it has been observed that ME treatment shows an increase life span, and a decrease in the tumor volume and viable tumor cell count in the EAC tumor hosts. Cytological studies have revealed a reduction in the mitotic activity, and the appearance of membrane blebbing and intracytoplasmic vacules in the treated tumor cells.

Yadav and Jain (1999) have reported that posto coital administration of aqueous extract of seed of *C. fistula* at the dose 500 mg/Kg/b.wt./day prevent pregnancy in all the treated female rats by virtue of anti-implantation property with antiestrogenic activity. In another experiment It has been concluded that the aqueous extract of seeds of *C. fistula* owing to its potent antiestrogenic nature alter the biochemical milieu of the reproductive tract
which led to change the normal status of the reproduction in female reproductive tract of rat and have produced significant antifertility effect (Yadav and Jain, 2009).

Hanif et al. (2006) have studied the use of fallen parts (leaves, branches, pods, stembark) of *C. fistula* as a naturally occurring bio-sorbent for the batch removal of Ni (II) in experimental conditions. They have showed that the maximum pH for efficient sorption of Ni (II) biomass for Ni (II) removal tends to be in order of leaves<stem bark<pods bark.

Mehdi et al. (2011) have studied larvicidal property of leaf extract of *C. fistula* mosquito along with delayed morphogenetic effect. It exhibits IGR activity pertaining to its effect on growth and development and these compounds may be used as a solution for mosquito problem in the developing countries.

Govindrajan et al. (2009) have tested the leaf extract of *C. fistula* using different solvent viz, methanol, benzene and acetone for the larvicidal, ovicidal and repellent activity against *Aedes aegypti*. They have showed that the crude extract of *C. fistula* serve as a potential larvicidal, ovicidal and repellent agent against Chikungunya vector mosquito, *Aedes aegypti*.

Ramesh et al. (2010) have evaluated the anti-urolithiatic activity of the wood bark extracts of *C. fistula* in sodium oxalate induced uralithiasis in wistar rats model. They have found that methanolic and aqueous extracts of *C. fistula* have been significantly increased urine output and elimination of sodium and chlorides when compared to normal group. Histopathological evaluation shows the maximum prevention of crystal deposition at the dose of 100 mg/kg compared to 200 mg/kg.

Hernandez and Leonido (2011) have studied that the methanol extract of *C. fistula* shows hypolipidemic activity in diet-induced lipidemia in mice. Treatments with 3.0% *C. fistula* significantly lower the body weight and weight of para material fat in mice.
Khatib et al. (2010) have reported the cardio protective effect of the methanolic extract of *C. fistula* (MECB) bark against doxorubicin (DXR) induced cardio toxicity in wistar rats and have showed that rats treated with MECB at a dose of 400 mg/kg significantly decreases the elevated levels of serum enzymes. Decrease in histological disturbances and electrocardiogram changes to normal myocardium functioning have been also noticed.

Karthikeyan and Gobianand (2010) have studied the antiulcer activity of ethanolic leaf extract (ELE) of *C. fistula* against pylorus legation-induced gastric ulcer. Ranitidine (30mg/kg body weight) and ELE at different doses have administered orally in different groups of rats, 1 hour prior to pyloric ligation. Four hours after pyloric ligation, the gastric juice was collected for evaluation of various parameters. The antiulcer activity of ethanolic extract has been evidenced by the significant attenuation of gastric volume, pH, free acidity, and total acidity in the gastric juice. A higher dose of ELE (750 gm/kg b.w.) produces maximum antiulcer activity comparable to ranitidine treatment.

Kalantri and Zsuga (2011) have studied the efficacy of a crude hydro-alcoholic extract of *C. fistula* fruit to protect the kidney against bromobenzene-induced toxicity in mice. A significant effect have observed by using 200, 400, 600 and 800 mg/kg of *C. fistula* fruit extract followed by 460 mg/kg bromobenzene for 10 days. On 11th day, the mice has been sacrificed and blood samples have been examined and found that bromobenzene induced nephrotoxicity reflected by the *C. fistula* fruit extract. The nephroprotective, effect of the *C. fistula* fruit extract has been confirmed by the histological examination of the kidneys.

Ziyaurrahman et al. (2011) have investigated that the hydroalcoholic extract of *C. fistula* leaf extract has been found to possess significant neuropathy activity. *C. fistula* leaf was unable to protect the animals from acrylamide while it was able to reverse alcohol induced peripheral
neuropathy in dose dependant manner in the rats. This study have been confirmed that *C. fistula* can be of immense importance in the amelioration of the mono neuropathy in the human beings.

2.8 Immunomodulators

An immunomodulator is a substance (e.g. a drug) which has an effect on the immune system; it can be defined as a substance which is biological or synthetic origin, having properties to modulate i.e. stimulate or suppress any of the components of the immune system. Medicinal plants are believed to enhance the natural resistance of the body to infections. A plethora of plant derived materials (proteins, lectins, polysaccharides, etc.) have been shown to stimulate the immune system. Some of the plants with established immunomodulatory activity are *Viscum album*, *Panax ginseng*, *Asparagus racemonsus*, *Azadirachta indica*, *Tinospora cordifolia*, *Polygala senega*, *Ocimum santum*, *Withania somnifera*. *Cassia fistula* and some other plants have been studied as a one of the member of group of immunomodulators against viral infection and malignancies and were found to contain plant interferons. (Anonymous, 1999).

Immunomodulatory agents of plant and animal origin increase the immune responsiveness of the body against pathogens by activating the non-specific immune system. However, there is a need to subject such medicinal plants to systematic studies to substantiate the therapeutic claims made with regard to their clinical utility (Fulzele, 2003). Recently, there is an enthusiasm towards exploration of a novel group of compounds from natural sources that modulate the immune response of living systems and influence the disease process (Gulati, 2002).

**Immunomodulatory properties of *C. fistula***

Ali *et al.* (2008) have studied the humoral effect of *C. fistula* and its synergestic antimicrobial combination with amoxicillin named ‘Amoxy-cassia’ (patent # 1371240) on BALB/C mice. Mice immunized with sheep RBCs and treated with *C. fistula* fruit, amoxy cassia, amoxicillin and normal saline.
Number of activated anti-SRBC producing cell in spleen calculated by haemolytic plaque assay and antibody titer in blood. It has been measured by haemagglutination test on past-immunized day 4, 6, 8, 10 in all treated animals and have observed that amoxy-cassia and water extract of fruit of C. fistula stimulate immune system by activating large number of anti RBC producing cells.

Das et al., (2008) have studied Aragvudha fruit pulp (C. fistula) has significant Kusthanghna activity (anti-eczema). Raised serum IgE level is the commonest immunological marker for eczema and they have found that all the treated patients with (Churna and lepa) fruit of C. fistula shows a significant decrease in serum IgE level and a significant relief has been found in all the treated patients.

Other species of Cassia have been studied for their immuno modulatory activity. Chakraborty (2009) have revealed that methanolic extract of C. auriculata shows a significant stimulation of cell mediated immunity with a dose of 50 and 100 mg/kg. In this experiment the humoral response to sheep RBCs has been unaffected.

Oladunmoye (2007) have revealed that the ethanolic extract of the leaf of C. alata has impressive immuno stimulatory activity on albino rat dosed with Staphylococcus aureus. They have observed a significant increase in the white blood cells in comparison to untreated rats.

Tilwari et al. (2011) have studied that daily the administration of alcoholic extract of C. tora (400 mg/kg) shows significant (P<0.05) effect compared with control but no significant effect has been observed at the lower doses. They have also studied delayed type hypersensitivity (DTH) response and have found that C. tora (400 mg/kg) shows significant effect.

### 2.9 Cytokines

Modulation of cytokine secretion may offer novel approaches in the treatment of a variety of disease. One strategy in the modulation of cytokine
expression may be through the use of herbal medicines. A class of herbal medicine called the immunomodulators alters the activity of immune function through the dynamic regulation of informational molecules such as cytokines (Burns et al., 2006). Cytokines are soluble glycoproteineous non immunoglobulin bio molecules secreted by living cells of the host. Which act non enzymatically in subnanomolar concentration through specific receptors expressed on target cells. They constitute the fourth major class of soluble intracellular signaling molecules (inter cellular messenger for cell to cell communication) along with endocrine hormones, growth factors and neurotransmitters. Different names have been used depending on their origin such as lymphkines produced from monocytes. According to their activity they are also names as interferon, growth and differentiation factors & colony stimulating factors. In order to simplify the terminology, the term interleukin has been accepted. On the basis of inflammatory reaction, there are two main groups of cytokines proinflammatory and anti-inflammatory. Overall cytokines can be grouped into following families.

1. Interferons
2. Chemokines
3. TNF family
4. Proteins (interleukin) IL2, IL3, IL4 etc.
5. Polypeptide growth factors
6. Migration inhibition factor:

Cytokines are produced by large variety lymphoid and non lymphoid cells. Non lymphoid cells include macrophages, dendrite cells, fibroblasts, keratinocytes, endothelial cells and variety of transformed cell lines. Among lymphoid cells, TH1 and TH2 subpopulations and Tc cells are the producer of cytokines. Overall TH cells including TH1 & TH2 subsets and macrophages are the principal cytokine producing cells (Burns et al., 2006).

**Interferons**

Interferons have been identified as antiviral agents in the year 1957 by Issacs and Lindemann. Three types of interferon alpha, beta and gamma
are identified. Interferon have demonstrated activity in infectious autoimmune disease and selected cancer. IFN are produced by the body in response to viral infections and tumors, and to regulate immunity. Interferons are classified according to cellular origin and the type of receptors they bind. Interferon cell surface receptors type 1; although they have different binding affinities, they have similar biological effects (Pfeffer et al., 1998). Interferon is type II, since it binds only to type 2 receptors. Leukocytes produce Interferon, fibroblasts produce IFN, and activated T-cells and natural killer cells produce Interferon (Balkwill, 1989). Type 1 IFNs induce antiproliferative and antiviral activity. IFN-γ has been found to increase bone resorption and hematopoesis. Interferons are used in the treatment of hepatitis B and C, Malignant melanoma, follicular lymphoma and AIDS related kaposi sarcoma (Varshney, 2012).

Cada and Covington (2000) have revealed that interferon have overlapping but clearly distinct biological activities. Type I interferon induce intiproliferative and antiviral activity. Type II interferon has weaker antiviral activity, more potent immunomodulator properties, and binds to completely different receptors than type I interferons. IFN also has a different range of immune functions, including macrophage activation.

Human IFN-γ is a 35 kD protein containing 143 amino acid residues. IFN-γ upregulates ICAM-I expression on endothelial cells and has become a primary maker for Th-I like immune response research (Agrawal et al., 2008). IFN-γ is secreted by ThI cells, Tc cells, dendritic cells and NK cells. IFN-γ has antiviral immunoregulatory, and anti-tumour properties. It alters transcription in up to 30 genes producing a variety of physiological and cellular responses. IFN -γ is the hallmark cytokine of Th1 cells (whereas Th2 cells produce IL-4 and Th17 cells produce IL-17). NK cells and CD8+ cytotoxic T cells also produce IFN-γ (Cherng et al., 2008).

Cherng et al. (2008) have evaluated the immunostimulatory activities of four anthraquinones of C, tora (aloemodin, emodin, enrysophenol and rhein) on human peripheral blood mononuclear cells (PBMC).
Interleukins

Interleukins are a subset of a larger group of cellular messenger molecules called cytokines, which are modulators of cellular behavior. Like other cytokines, interleukins are not stored within cells but are instead secreted rapidly and briefly in response to a stimulus, such as an infectious agent. Once an interleukin has been produced, it travels to its target cell and binds to it via a receptor molecule on the cell’s surface. This interaction triggers a cascade of signals within the target cell that ultimately alter the cell’s behavior (Kuby, 2003).

The first interleukin was identified in the 1970s. There are at least 33 type of interleukins reported in literature. Initially investigators believed that interleukins are made chiefly by leukocytes (white blood cells) to act primarily on other leukocytes, and for this reason they named them interleukins, meaning “between leukocytes”. Because leukocytes are involved in mounting immune responses, interleukins were thought to function only as modulators of immune functions. Although this is an important function of interleukins, it is now known that interleukins also are produced by and interact with a host of cells not involved in immunity and are involved in many other physiological functions (Encyclopedia Britannica 2007., Kuby, 2003., Tizzard, 1992).

Interleukins-10 (IL-10)

Interleukin-10 originally known as Cytokine Synthesis Inhibitory Factor (CSIF) is a 18.5kI) protein that shares over 80% sequence homology with Epstein –Barr virus protein (BCRFL). IL-10 can inhibit the synthesis of certain cytokines IL-I, IL-2, IL-6, IL-8, IL-12, GM-CSF and TNF by stimulated macrophages, NK cells and T cells co-stimulate the proliferation of B cells and their differentiation into antibody-producing cells which can express high level of IgM, IgG and IgA antibodies (Agrawal et al., 2008). It is mainly expressed in monocytes and type 2 T helper cells (T_H2), mast cells, and CD4 + CD25 regulatory T cells and also in certain subset activated T cells and B cells. It is released by cytotoxic T-cells to inhibit the actions of NK cells during the immune response to viral infection (Cherng et al., 2008).
Table 1: Effects of different plants on IFN-γ induction are listed below

<table>
<thead>
<tr>
<th>Cytokins</th>
<th>Plant</th>
<th>Model</th>
<th>Direction of effect</th>
<th>Author/Date</th>
</tr>
</thead>
<tbody>
<tr>
<td>IFN-γ</td>
<td>Acalypa walkesiana</td>
<td>In vitro, Human</td>
<td>Increase</td>
<td>(Bussing et. al., 1999)</td>
</tr>
<tr>
<td></td>
<td>Acanthopanax gracilistylus</td>
<td>In vitro, Human</td>
<td>Decrease</td>
<td>(Shan et. al., 1999)</td>
</tr>
<tr>
<td></td>
<td>Allium satvum</td>
<td>In vitro, Human</td>
<td>Decrease</td>
<td>(Hodge et. al., 2002)</td>
</tr>
<tr>
<td></td>
<td>Ananus comosus (Bromelain)</td>
<td>In vitro, Murine</td>
<td>Increase</td>
<td>(Engwerda et. al., 2001)</td>
</tr>
<tr>
<td></td>
<td>Cissampelos sympodialis</td>
<td>In vitro, Murine</td>
<td>Decrease</td>
<td>(Piuvezam et. al., 1999)</td>
</tr>
<tr>
<td></td>
<td>Cordyceps cicanda (Fruit body)</td>
<td>In vitro, Human</td>
<td>Increase</td>
<td>(Weng et. al., 2002)</td>
</tr>
<tr>
<td></td>
<td>Cordyceps cicada (Larvae)</td>
<td>In vitro, Human</td>
<td>Decrease</td>
<td>(Weng et. al., 2002)</td>
</tr>
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<td></td>
<td>Emblica officinalis</td>
<td>In vitro, Murine</td>
<td>Increase</td>
<td>(Sai ram et. al., 2001)</td>
</tr>
<tr>
<td></td>
<td>Grifola frondosa</td>
<td>In vitro, Murine</td>
<td>Increase</td>
<td>(Kodama et. al., 2002)</td>
</tr>
<tr>
<td></td>
<td>Panax ginseng</td>
<td>In vitro, Murine</td>
<td>Increase</td>
<td>(Shon et. al., 2002)</td>
</tr>
<tr>
<td></td>
<td>Polygala tenuifolia</td>
<td>In vitro, Murine</td>
<td>Decrease</td>
<td>(Hong et. al., 2002)</td>
</tr>
<tr>
<td></td>
<td>Rauwolfia serpentine</td>
<td>In vitro, Murine</td>
<td>Increase</td>
<td>(Hong et. al., 2002)</td>
</tr>
<tr>
<td></td>
<td>Withania somnifera</td>
<td>In vitro, Murine</td>
<td>Increase</td>
<td>(Davis and Kuttan 1999)</td>
</tr>
</tbody>
</table>
Table 2: Effects of different plants on IL-10 induction are listed below.

<table>
<thead>
<tr>
<th>Cytokins</th>
<th>Plant</th>
<th>Model</th>
<th>Direction of effect</th>
<th>Autor/Date</th>
</tr>
</thead>
<tbody>
<tr>
<td>IL-10</td>
<td><em>Allium sativum</em></td>
<td><em>In vitro, Human</em></td>
<td>Decrease</td>
<td>(Hodge <em>et al.</em>, 2002)</td>
</tr>
<tr>
<td></td>
<td><em>Cissampelos sympodialis</em></td>
<td><em>Invitro, Murine</em></td>
<td>Decrease</td>
<td>(Piuevezam <em>et al.</em>, 1999)</td>
</tr>
<tr>
<td></td>
<td><em>Echinacea purpurea</em></td>
<td><em>In vitro, Human</em></td>
<td>Decrease</td>
<td>(Piuevezam <em>et al.</em>, 1999)</td>
</tr>
<tr>
<td></td>
<td><em>Silybum marianum</em></td>
<td><em>Invitro, Murine</em></td>
<td>Decrease</td>
<td>(Hodge <em>et al.</em>, 2002)</td>
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</table>