REVIEW OF LITERATURE:

Debashis et al., 2002 reported that due to imbalance between aggressive and cytoprotective factors cause development of gastric ulcer. Aggressive factors divided into two classes exogenous and endogenous. Hydrochloric acid, leukotrienes, reflux bile, reactive oxygen species and pepsin are endogenous factor Emotional stress, tension, H. pylori, and pepsin and gastric acid secreted by non-steroidal anti-inflammatory (NSAID) drugs, ethanol are exogenous factors. Mucosal bicarbonate barrier, mucosal blood flow, surface active phospholipid, prostaglandin, cell renewal and migration, antioxidants and antioxidant enzymes are cytoprotective factor. Lipid peroxidation caused by ‘OH is increase in gastric lesion induced by ethanol.

Andrade et al., 2007 described that NSAID inhibiting prostaglandin synthetase through the cyclooxygenase pathway. Prostaglandin play a important role in stimulating the secretion of bicarbonate and mucus, maintaining mucosal blood flow and regulating mucosal cell turnover and repair.

Cordia dichotoma

Kirtikar et al., 1935 reveal that Cordia dichotoma, the fragrant manjack or the bird lime tree, is a plant species in the genus Cordia. It is called gunda or tenti dela in Hindi and lasura in Nepali

Wassel et al., 1990 Studied and showed presence of flavonoids in extracts of Cordia dichotoma Forst.f. fruits tested and showed significant anti-ulcer and cytoprotective effects against gastric ulcer in rats. The anti-ulcer effect of extracts of Cordia dichotoma Forst.f. fruits (300mg/kg body weight) was studied in albino rats of Wistar strain using three different models i.e. pyloric ligation, aspirin and indomethacin induced ulcers.

Alarcon., 1994 reveal and did chemical screening of both the leaves and the fruits showed the presence of pyrrolizidine alkaloids, coumarins, flavonoids, saponins, terpenes and sterols.

The extract produced significant writhing inhibition in acetic acid induced writhing in mice at the oral dose of 500 mg/kg body weight respectively (P<0.001), which was comparable to the standard drug diclofenac sodium at the dose of 25 mg/kg of body weight. When tested for its antibacterial effects disc diffusion method, it significant zone of inhibition of against both Gram negative and Gram positive bacteria when tested for toxicity using brine shrimp lethality bioassay, the extract showed potent activity against the brine shrimp Artemia salina (LC50: 20
g/ml and LC90: 180 g/m). The overall results tend to suggest the analgesic, antibacterial and cytotoxic activities of the extract.

Alarcon., 1994 reveal and did chemical screening of both the leaves and the fruits showed the presence of pyrrolizidine alkaloids, coumarins, flavonoids, saponins, terpenes and sterols. Larson et al., 1998 reveal that the ethanol extract of the leaves reduced acetylcholine-induced contractions of guinea-pig ileum. Ethanol extracts from fruits and leaves showed significant antioxidant activities due to the carotenoids but no antimicrobial activity against gram-positive or gram-negative bacteria. Medicine: Seeds of the species are anti-inflammatory, 2 compounds alpha-amyrin and 5-dirhamnoside have been isolated.

Yang et al., 2002 isolated Four flavonoid glycosides (robinin, rutin (rutoside), datiscoside and hesperidin), a flavonoid aglycone (dihydrorobinetin), and 2 phenolic derivatives (chlorogenic acid and cafféic acid). As well as the petroleum ether and alcoholic leaves extracts showed significant analgesic, anti-inflammatory and anti-arthritic activities in tests with rats.

Ilhami et al., 2004 describe Flowers are short-stalked, bisexual and white in colour, appear in loose corymbose cymes. The fruit is a yellow or pinkish-yellow shining globose or ovoid drupe seated in a saucer-like enlarged calyx. It turns black on ripening and the pulp gets viscid. The hard stone is 1-4 seeded. The generic name honours a 16th century German botanist, Valerius Cordus.

Sharma et al., 2007 describe in book that Cordia dichotoma L. family Boraginaceae small to moderate-sized deciduous tree with a short bole, short crooked trunk and spreading crown. The stem bark is greyish brown smooth or longitudinally wrinkled. leaves simple, entire and slightly dentate, elliptical-lanceolate to broad ovate with a round and cordate base. These flowers are followed by 1 in (25mm) long dull pinkish edible fruits with sticky flesh

Thirupathi et al., 2007 studied the effect of methanolic extract of C. dichotoma (MCD) was prepared by the maceration of leaf powder. The effect of the extract on Aspartate amino transferase (AST), Alanine amino transferase (ALT), Alkaline phosphatase (ALP), serum bilirubin(TBR), glutathione, lipid peroxide(MDA) and total antioxidants levels in CCl4 induced liver damage in rats are seen. They found The hepatoprotective properties of Silymarin have been related to the inhibition of lipid peroxide formation or scavenging of free radicals generated by microsomal ethanol oxidations. The extract of C. dichotoma also produced hepatoprotective
activity similar to silymarin and so its action may also be due to inhibition of lipid peroxide formation. It also increased the total antioxidant levels to some extent. The hepatoprotective action combined with antioxidant activity may have a synergistic effect in preventing the initiation and progress of hepatocellular diseases.

Singh et al., 2010 describe that a common theme which underlies etiology of several degenerative disorders is free radical induced stress. Free radicals prime the immunomodulatory response, recruit inflammatory cells and are innately bactericidal. In the body, excess production of free radicals affects lipid cell membranes to produce lipid peroxides and reactive oxygen species (ROS) which leads to decline in membrane fluidity and many biological changes, such as DNA damage, ageing, heart disease and cancer. The carried out to investigate the free radical scavenging potential of methanolic extract of seeds and leaves of Cordia dichotoma using in-vitro models viz. DPPH and hydrogen peroxide model. These models demonstrate positive antioxidant activity in a concentration dependent manner and demonstrate that highest concentration exhibits highest (100 g/ml) antioxidant activity.

Swami et al., 2010 studied effect of aqueous leaves extract of Cordia dichotoma on blood glucose levels of normoglycemic & alloxan-induced diabetic wister rats. Three doses of the extract (250 mg/kg; 500 mg/kg and 1000 mg/kg) were administered orally. The 500 mg/kg extract of Cordia dichotoma did not show any significant change in the blood glucose levels in normoglycemic and 250 mg/kg did not show any significant change in the blood glucose levels in alloxan Induced Diabetic Wister rats, when compared to untreated control. The dose 500 & 1000 mg/kg of extract showed a significant (p<0.5) decrease in blood glucose levels after 4, 8 and 24 hours.

Jain et al., 2010 evaluated the antidepressant effect of ethanolic and aqueous extracts of Cordia dichotoma leaves by using behavioural animal models. In their study they had selected behavioural despair models namely forced swimming and tail suspension tests. The main findings of present investigations suggests that the above extracts posses antidepressant activity in rat forced swim test,tail suspension test in mice and open field test in rats. The acute toxicity study were conducted as per OECD guideline 420.It was found that the ethanolic and aqueous extracts even at 2000mg/kg dose had not shown any mortality. Hence, it confirms that it is practically non - toxic in nature. Ethanolic and aqueous extracts of Cordia dichotoma leaves has
dose dependant antidepressant activity at dose 200mg/kg (low dose) and dose 400mg/kg (high dose).
**Caesalpinia bonduc**

*Kirtikar et al., 1993* describe *Caesalpinia bonduc* (CB), also known as *Caesalpinia crista*, is an important medicinal herb reported in Ayurveda belonging to family Caesalpiniaeae. It is found throughout India and tropical countries of the World. The plant is up to 15 m in height, found up to an altitude of 1,000 m in Himalaya and wild throughout the plains of India. Also, found particularly along the seacoast, and throughout the hotter parts of India, Burma and Sri Lanka. The roots are considered febrifuge and anthelmintic, they are much used as an astringent in leucorrhoea, eye diseases, and hyperacidity, ulceration.

*Iyenger et al., 1995* isolated from Ethanolic extracts of bark of *Caesalpinia bonduc* (Fabaceae) yielded two new homoisoflavonoids, 6-O-methylcaesalpinianone and caesalpinianone along with five known natural products namely- hematoxyloil, 6′-O-acetylloganic acid, 4′-O-acetylloganic acid stereochenoil A, 2-O-β-d-glucosyloxy-4-methoxybenzenepropanoic acid

*Peter et al., 1997* isolated Two new cassane diterpenes, named caesaldekarins F and G, were isolated and identified from the roots of *Caesalpinia boduceilla*. The recently reported caesaldekarin C was also isolated from the roots of this plant.

*Sabir et al., 2001*. Four triterpenoids and methanol extract from the seeds of *Caesalpinia bonducilla* have been shown to possess a wide range of inhibiting activity against both gram-positive and gram-negative bacteria.

*Parameshwar et al., 2002* reported the seed kernel powder was reported to have hypoglycaemic activity in experimental animals. Four extracts (petroleum ether, ether, ethyl acetate, and aqueous) were prepared from the seed kernels and tested for their hypoglycaemic potentials in normal as well as alloxan-induced diabetic rats. In normal rats, only ethyl acetate and aqueous extracts showed a minimum significant hypoglycaemic effect, compared to that of glibenclamide. In diabetic rats, the non-polar extracts i.e. the ether extract showed a marginal anti-diabetic activity, while the petroleum ether extract failed to show significant hypoglycaemic effect, besides, reversing the diabetes induced changes in lipid and liver glycogen levels. However, both the polar extracts (ethyl acetate and aqueous) as well as glibenclamide, showed the hypoglycemic effect. Since both the polar extracts were, chemically, found to contain triterpenoidal glycosides, it was postulated that they might be the active principles contributing to the anti diabetic actions of the plant.
Chakrabarty et al., 2003 showed that showed significant blood sugar lowering effect of CB in type 2 diabetic model.

Gupta et al., 2004 established anti-tumour effect of the methanol extract of CB leaves (MECB) in the Ehrlich ascites carcinoma (EAC)-bearing Swiss albino mice. The extract was administered at the doses of 50, 100, and 200 mg/kg body weight per day for 14 days after 24h of tumor inoculation. The study dealt with the effect of MECB on the growth of transplantable tumor, life span of EAC-bearing hosts, Review of Literature Dept. of Pharm. Sci., Saurashtra University, Rajkot, Gujarat, India 66 haematological profile, and biochemical parameters such as lipid peroxidation (LPO), glutathione content (GSH), superoxide dismutase (SOD), and catalase (CAT) activities. MECB caused significant (P <0.01) decrease in tumor volume, packed cell volume, and viable cell count; and it prolonged the life span of EAC-tumor bearing mice. MECB significantly (P < 0.05) decreased the levels of lipid peroxidation and significantly (P < 0.05) increased the levels of GSH, SOD, and CAT. The MECB was found to be devoid of conspicuous short-term toxicity in the mice when administered daily (i.p.) for 14 days at the doses of 50, 100, 200, and 300 mg/kg. The treated mice showed conspicuous toxic symptoms only at 300 mg/kg. The results indicated significant antitumor and antioxidant activity of MECB in EAC-bearing mice.

Archna et al., 2005 subjected ethanolic extract (70%) of CB seed kernel for its antipyretic and antinociceptive activities in adult albino rats or mice of either sex at 30, 100, and 300 mg/kg orally. The extract demonstrated marked antipyretic activity against Brewer’s yeast induced pyrexia in rats. The extract showed significant central analgesic activity in hot plate and tail flick methods.

Archna et al., 2005 established analgesic effect of the plant in both acetic acid-induced writhing test in mice and Randall-Selitto assay in rats. It was also shown that plant significantly inhibited the formalin induced hind paw licking in mice.

Shukla et al., 2008 established anti-inflammatory activity of the plant. Various concentrations of the seed oil of CB (100, 200, and 400 mg/kg orally) were tested in carrageenan-induced rat paw edema, brewer’s yeast induced pyrexia, acetic acid-induced writhing and hot plate reaction time in experimental rats to assess the anti-inflammatory,
antipyretic and analgesic activities. The paw volumes, pyrexia and writhes in experimental rats were reduced significantly (P < 0.05) as compared to that of control, and hot plate test showed significant licking effect in rats.

**Gaur et al., 2008** showed that the crude extract of the plant produced fall in microfilaria (mf) count in L. sigmodontis-cotton rat model.

**Shukla et al., 2009** reported immunomodulatory activity of the seeds of the plant. Oral administration of ethanolic seed extract of CB (200-500 mg/kg) evoked a significant increase in percent neutrophil adhesion to nylon fibers as well as a dose dependent increase in antibody titre values, and potentiated the delayed type hypersensitivity reaction induced by sheep red blood cells. Also, it prevented myelosuppression in cyclophosphamide drug treated rats and showed good response towards phagocytosis in carbon clearance assay. These results indicated that CB possesses potential Immunomodulatory activity and has therapeutic potential for the prevention of autoimmune diseases.

**Moringa oleifera**

**The wealth of india.,1988** book describe *Moringa oleifera* belonging to family Moraginaceae is a small or medium sized tree, about 10 m, high found wild in the sub-himalayan tract and cultivated all over the plains of India.

**PDR for herbal medicines,1993** describe *M.oleifera* fruit is a hanging capsule opening on 3 sides, up to 1.2 m long and triangular with 9 ribs. The seeds are triangular, light brown to black, with 3 thin, whitish wings, approximately the size of a hazelnut.

**Dahot ,1998** taken Three fractions from the leaves of *Moringa oleifera* were obtained on Sephadex G-25 column chromatography. An antibacterial action of small protein/peptide was tested against *E. coli* *Kl. aerogenes, Kl. pneumoniae, S. aureus, and B. subtilis. Moringa oleifera* leaves were dried at room temperature and were ground into fine powder with mortar and pestle. The dried powder of leaves (50 g) was defatted with 150 ml of diethyl ether at room temperature for 8 hours and filtered with Whatman no. 1. The residue was extracted with 33 ml cold distilled water and centrifuged (Kubota refrigerated centrifuge, Japan) at 6000 rpm. The supernatant was transferred to 100 ml volumetric flask and this procedure was repeated twice and volume was made upto the mark with distilled water. Small proteins/peptides were precipitated by the addition of two fold acetone. The precipitates were dissolved in sterilized distilled water and
dialyzed over night. There observation provides strong circumstantial evidence that small proteins/peptides play an important role in plants of antimicrobial defence system

Chatterjee ,2003 stated in his book *M.oleifera* is well known herb used in many pathological condition and mentioned in many ancient literature for its useful action in dysthria, appetizing, stomachic and heals ulcer. Fruits contain minerals, vitamins and amino acids. Plant also showing presence of quercetin, kaempferol.

Dahiru et al.,2006 studied The effect of aqueous extract of *Moringa oleifera* leaf was studied on experimentally induced gastric ulceration in rats. Pretreatment with extract 200, 300 and 400 mg/kg bw reduced the characteristic lesions induced by indomethacin compared to untreated control group in a dose dependent manner. The effects observed could be due to the action of one or more of the phytochemicals present in the leaf extract. Phytochemical screening of the leaf extract of Moringa oleifera revealed the presence of alkaloids, glycosides, phenols, saponins, tannins, volatile oils and hydrolysable tannins. The leaf extract was found to protect the gastric mucosa against indomethacin effect in a dose dependent manner. Phytochemical constituent of the leaf extract of Moringa oleifera (tannins and flavonoids) that reduced initiation and perpetuation of ulceration may be responsible for the observed effects. The leaf extract thus has thepotential of an antiulcerogenic agent, which suggest it’s used in traditional medicine.

Devaraj et al.,2007 reported The effect of different extracts of leaves and fruits of *Moringa oleifera* Lam. (Moringaceae) on gastric and duodenal ulcers was evaluated by using different gastric ulcer models and cysteamine-induced duodenal ulcer method. The acetone extract and methanol extract of the leaves produced gastric antisecretory effect in pylorus-ligated rats and showed gastric cytoprotective effective in ethanol-induced and indomethacin-induced gastric ulcers. The leaf extracts also produced a significant reduction of stress-induced gastric ulcers and cysteamine-induced duodenal ulcers. None of the extracts of the fruits showed any significant antiulcer effect. It was concluded that leaves of *Moringa oleifera* increase healing of gastric ulcers and also prevent the development of experimentally induced gastric ulcers and duodenal ulcers in rats.

Chuang et al.,2007 evaluated the therapeutic properties of the seeds and leaves of *Moringa oleifera* Lam as herbal medicines. Ethanol extracts showed anti-fungal activities in vitro against
dermatophytes such as *Trichophyton rubrum*, *Trichophyton mentagrophytes*, *Epidermophyton Xoccosum*, and *Microsporum canis*. GC–MS analysis of the chemical composition of the essential oil from leaves showed a total of 44 compounds. Extracted compounds interacted with the lipid bilayers in membranes leading to the separation of the two membranes (outer and inner membranes). Subsequently, water dips into the cell, which causes cell to swell more and leads cell to death.

**Paulo et al., 2009** reported biological effects of the extract of *Moringa oleifera* seeds (WEMOS) were assessed on eggs and 3rd instar larvae of *Aedes aegypti* and on its toxicit upon laboratory animals (*Daphania magna*, mice and rats) Crude WEMOS showed a LC50 value of 1260 µg/ml, causing 99.2± 2-9% larvae mortality within 24hr at 5200 µg/ml though this larvicidal activity has been lost completely at 80°C /10 min. Acute toxicity evaluation on daphnids and mice pointed out low toxicity. Study clearly demonstrated that water extract of *Moringa oleifera* seeds have lethal action against *Aedes aegypti* larvae and low toxic effects on laboratory animals, which is in agreement with the literature.

**Sudha et al., 2010** investigated the immunomodulatory action of methanolic extract of *Moringa oleifera* (MEMO) in an experimental model of immunity. The cellular immunity was evaluated using neutrophil adhesion test, cyclophosphamide induced neutropenia and carbon clearance assay, whereas, humoral immunity was tested by mice lethality test, serum immunoglobulin estimation and indirect haemagglutination assay in animals. Administration of MEMO (250 and 750 mg/kg, po) and Ocimum sanctum (100 mg/kg, po) significantly increased the levels of serum immunoglobulins and also prevented the mortality induced by bovine *Pasteurella multocidain* mice. They concluded that MEMO stimulate both cellular and humoral immune response. However, low dose of MEMO was found to be more effective than the high dose.

**Tende et al., 2011** determined the hypoglycemic effect of *Moringa oleifera* [family: Moringaceae] ethanolic extract in normal (normoglycemic) and STZ induced diabetic Wistar rats. In one set of experiment, graded doses of the leaves extract (250 and 500 mg/kg i.p.) were separately administered to groups of fasted normal and fasted STZ diabetic rats. The hypoglycemic effect of the ethanolic leaves extract as compared with that of insulin 6 i.u/kg in fasted normal and STZ diabetic rats. Following treatment, relatively moderate to high doses of *Moringa oleifera* (250 and 500 mg/kg i.p.) produced a dose-dependent, significant reduction
(p<0.05) in blood glucose levels of fasted STZ diabetic rats only. The ethanolic extract of the leaves of *Moringa oleifera* possesses hypoglycemic activity in STZ induced diabetic Wistar rats only.