5.1. Summary:

The stomach is a pouch like muscular organ. Upper side of the stomach, esophagus is present and the lower side duodenum is present. The stomach is dividing into 3 part, fundus, body and pyloric end. The fundus is grayish in color. The body areas help in churning movement with the greater curvature and lower curvature. Distal area is known as pyloric end. It having pyloric sphincter which control the passes of food into the small intestine. Cardiac end means the end of the stomach which is followed by esophagus. The pyloric sphincter open in first part of small intestine - duodenum.

The stomach divide into two curvature a) lesser and greater. The stomach has four coats; serous (peritoneal), muscular, sub-mucosa, and mucous coat. The thick muscular has three layers; outer longitudinal, inner circular and oblique layer is visible in cardiac end it extends into the lesser curvature. Obviously, gastric muscles are smooth muscles. The circular layer of the gastric muscles is particularly thick in pyloric area.

The gastric mucosa is bulky, at the time of empty stomach and make longitudinal fold known as rugae. But at the time of food filled stomach, the rugae disappear. Normally, over the mucousa of the stomach, lies thick viscid mucus.

The gastric mucosa, according to modern research is divided into three areas: cardiac glandular area, oxyntic glandular areas and pyloric glandular areas. They are also called fundus, body and pyloric areas respectively.
Stomach contains various glands like gastric glands and oxyntic glands which having major role in the gastric juice secretion. Gastric juice includes 99% of gastric juice and 1% of solid materials which contains: Inorganic-HCl, HCO₃⁻ and Organic-pepsinogen, mucus, intrinsic factor. Major function of gastric juice include: digestive, antimicrobial, protective and absorption vit-B12 that due to intrinsic factor.

Three chemicals gastrin, histamine, and acetylcholine released from vagal parasympathetic fibers acting as neurotransmitter, stimulate HCl secretion from parietal cells. The parietal cells containing receptors of gastrin, histamine and acetylcholine. Gastrin and acetylcholine combine with their respective receptors leads to rise of Ca²⁺ ion concentration within the cell, abbreviated [Ca²⁺]. This causes increased H⁺, K⁺ ATPase activity; more HCl secretion. Combination of H with its receptor causes rise of intracellular cAMP causes rise in HCl emission.

Inhibition of HCl secretion is done by the somatostatine which secreted by the D-cells in pyloric glands. Somatostatine inhibits the parietal cells, G cells, ECL cells responsible for the HCl stimulations. Other gastric inhibitory hormones are secretin, cholicystokinn, gastrin inhibitory peptide. Majority of the community gets suffered by the peptic ulcer. At the stomach on lesser curvature and first part of the duodenum are common sites for peptic ulcers. Aggressive factor, consisting of acid pepsin mixture which, if left unopposed and allowed to act will digest the gastric mucosa, and mucosal barrier described earlier, that can defend gastric mucosa contrary to harsh deed of acid pepsin mixture. If aggressive factor become more powerful or mucosal barrier become weak, gastric mucosa will be damaged.

Gastric ulcer form by the secretion of gastric acid and against it decreases in the secretion of bicarbonate in gastric mucosa. Because of gastric ulcer sharp burning
pain is occur in epigastrin. In the cephalic phase of acid secretion excess amount of acid get secret and it will damage the epithelial layer of stomach.

Gastric ulcer may cause the nausea, vomiting where as its pain produce weight loss and anorexia. One forth percentage of people is suffering from gastric ulcer which causes hemorrhage some time. There is significantly rising in the complication and death because of gastric ulcers. Gastric ulcer is very usual disease; lots of people are affected by that in throughout the world. Because of that there is arising in the mortality rate. In United state four million people have peptic ulcer and each year 3,50,000 new cases reported. Allopathic treatment is base on the observation and etiology of disease is base on manifestation of an abnormal physiology.

However it has not been able to adequately helpful in the drug development discovery program to provide new molecules base on synthetic chemistry. Disillusioned by the non availability of drug to cure in chronic disease and failure of drugs in current use to give long term relief, that is why people are look after for alternative drug therapies as hope of a permanent cure. Unconfirmed and wrong claim of cure provided by traditional drugs leading to lots of misuse. Therefore it is a major area of interest to work on such claims and claims in literature of traditional drugs for exacts scientific search before they are give to humans.

It is fascinating to know that there is advance synthetic chemistry but we are fail to synthesize new molecule which having high therapeutic value and less adverse action than existing molecule. By searching in an ancient literature, identification of natural drug molecule used in local and tribal medicine pursue investigation into the phytochemical profile are emerging as new trend in drug discovery. Isolation of active molecule, finding of their chemical structure and testing of biochemical activity is also advance fame of work. On a basis of ancient literature and tribal medicine
very less work has been done and in India there is rich biodiversity so world researcher are eager to study on a dug use in India with hope that they may be potential source for the discovery of newer medicine.

In a treatment of gastric ulcer majority of patients are taking long term therapy ex; H2 blockers, proton pump inhibitors which having less chances of permanent cure. (Akram M. 2010) With the use of such a drugs help in healing, relieve pain and complications. Therapy includes following drugs like ranitidine, cimetidine, famotidine, prostaglandins, antacids, anticholinergics, omeprazole, etc. These all drugs are synthetic which is having many side effects; sometimes effects are unbearable for the patients. (Pharmaguide, 2006) All above drugs are give successful effect in treating and controlling peptic ulcer but still treatment is unsatisfactory due to lack of complete information about etiology and pathophysiology of disease. Drugs use in peptic ulcer having less of morbidity and mortality but may create many unlikeable reactions like gynecomastia, sterility, haemopoietic variations along with that higher chances of recurrence. It was observed that reactive oxygen species are main participants in many gastrointestinal diseases including peptic ulcer in recent studies.

In the last decade rise in awareness to growing biological concept result an increase interest in herbal formulation throughout world because it has been proved that herbal formulation is more advantageous than the synthetic drugs.(Narayan S. 2004) The polyherbal formulation may carries various effects like inhibition of acid secretion, decrease formation of free radical and erosion of mucosa etc. by its individual substance or may be by its synergistic effects.

In this research work, anti-ulcer and anti-secretory action of polyherbal formulation was carried out and evaluated. In this study *Dalbergia sissoo, Carissa carandas* and
Gymnema sylverstre drugs are extracted and using different solvent. After getting these solvent the anti ulcer study was performed. Select the one extract from each drug who having great anti ulcer activity and formulated different formulation using different possible probability. These formulations were evaluated for stability study and again for anti ulcer, anti secretory action.

The present research work was involved in different ulcer models get used like acetic acid induced ulcer model, pylorus ulcer model and stress induce ulcer models. Among this models, acetic acid induced ulcer model was found chronic and in that ulcer get produced by the acetic acid and drug was given for 10 days. On the 11th day rats get euthanized and ulcer index get counted and compared it with the standard and control. Another model is pylorus ligation in which ret get ligated on pyloric end of the stomach and gastric juice get collected. This pyloric juice used for different secretory action and compared it with standard. In the cold stress model the animals were placed in low temperature for estimated time. Due to this stress get developed and ulcer get formed in the stomach. Produced ulcer get compared with standard using ulcer index.

Dalbergia genus having 300 species all over world and about 25 species available in the India. In view of brightening and frequently fragrant wood, rich in aromatics show in timber trees Dalbergia are foreign. Fabaceae is a family of Dalbergia sissoo (D. Sissoo) also identified as Shisham local to Indian Subcontinent. Other than it is known as Indian rosewood, sheesham, tahli, sisu. Dalbergia sissoo is an expansive tree having stature of 25 meter and width of 2-3 meter. It has 15cm long rugged
takes off. Leaves are engraved having flyers are 3-5, substitute, 2.5 cm-3.6 cm in width. They are wide praise taper, glabrescent, petiolules 3-5mm long. Blossoms are whites pink in shading, 5-8mm long, pale white to dull yellow shading. Racemes 2.7-3.7cm long in short axillaries panicles. Its crown is fit as a fiddle; natural products are chestnut and case like shape which is 5-7.5cm × 8-13mm and having 1-4 seeds. Seeds are kidney fit as a fiddle having width of 6-8 × 4-5mm. (Orwa et al, 2009)

It is a huge deciduous tree found all through India, has been accounted for in people drug and is utilize basically as sexual enhancer, abortifacient, expectorant and anthelmintic. It is additionally use in as Anti- emesis, Anti- ulcers, leucoderma, loose bowels, stomach inconveniences and skin ailments, diabetes,( Singh N. and Jain K. 2010) abrasions, gonorrhea, pain relieving and antipyretic activities. Dried leave of Dalbergia sissoo is accounted for have antibacterial, hostile to protozoal, mitigating movement. (Taha S. and Abdul G. 1999)

Carissa Carandas has family Apocynaceae. (Khare P. 2007) It is otherwise called karamarda, karinkaara. It is local plant normally find in India, Malaysia, Shri-Lanka, Myanmar and Pakistan. The plant contain different cardiovascular glycosides, triterpenoidal- carisson and β-sitosterol were accounted by root separate. Alongside this it contain carissic corrosive, ascorbic corrosive, lupeol, glucose, serine, glutamine, alinine, valine, phenylalanine and glycnine. In conventional arrangement of solution, plant is utilized as an anthelmintics, astringents, starter, antipyretics, in biliary & stomach issue, ailment and infection of brain (Kirtikar R. 2005) furthermore indicates action against acidity. (Khare P. 2007) It was found that plant concentrate has cardiotonic, antipyretic and anti- viral activity. (Rajasekaran A. and Jayakar B,1999) Carissa carandas additionally indicate antibacterial, foragers of free radicals and inhibitors of xanthine oxidase, cell reinforcement, circulatory strain,
hepatoprotective, pain relieving and calming movement and it likewise valuable in hypoglycemic conditions. (Hasnain A. 1990; Bhaskar H, 2009)

*Gymnema sylvestre* belongs to family Asclepiadaceae(Khare CP 2007) it is also known as Madhunashini, Gudmar. It is native to India. This Plant leaves are being utilized as a part of India for more than 2000 years for treatment of madhumeha. Gudmar or sugar destroyer name is given depend on its function, eating leaves it destroy ability to destroy sweet test. Plant contains resins, saponins, stigmasterol, gymnemic acid, quercitol, betaine, choline and trimethylamine. *Gymnema sylvestre* is utilize in diuretic, stomachic, refrigerant, tonic, along with that it is use in heart disorder, leucoderma, inflammation, piles, curing burning sensation, bronchitis, asthama, biliousnessand ulser.

Gastric ulcer form by the secretion of gastric acid and against it decreases in the secretion of bicarbonate in gastric mucosa. Because of gastric ulcer sharp burning pain is occur in epigastrin. In the cephalic phase of acid secretion excess amount of acid get secret and it will damage the epithelial layer of stomach. Nowadays peoples change their lifestyle and they are get adapted for junk-food which can only fill the stomach without any nutrient supply. It can majorly damage the gastric intestinal track and form the gastric ulcer. Gastric ulcer can easily seen in the major population.

Gastric ulcer may cause the nausea, vomiting where as its pain produce weight loss and anorexia. One forth percentage of people is suffering from gastric ulcer which causes hemorrhage some time. There is significantly rising in the complication and death because of gastric ulcers. Gastric ulcer is very usual disease; lots of people are affected by that in throughout the world. Because of that there is arising in the
mortality rate. In United state four million people have peptic ulcer and each year 3,500,000 new cases reported.

In market there are lots of medicines have been used to treat GI ulcer like H\textsubscript{2} receptor antagonists frequently used for the gastric ulcer. But it having some adverse effect like pain, skin rash, weakness, arrhythmia. Another drug use for the gastric ulcer is proton pump inhibitors it may cause hyper gastinemia and atrophic gastritis. Another kind of drugs like antacids and anticholinergic drugs may causes the stomach disturbances, belching, constipation and there is risk of ulcer perforation, urinary retention, constipation, xerostomia, dry mouth, blurred vision, fluctuation in intra ocular presser.

Postaglandin analogues is another category of drug used in gastric ulcer. But when it can be used there may be a chances of abortion in pregnant woman, abdominal disturbances, uterine bleeding, dizziness, diarrhea, hypophosphatemia.

So there is always need for safer drug to treat gastric ulcer and herbal medicine is always good option to treat gastric ulcer because of drugs are more safe, freely available, less toxic and more important that they are more compatible with human body. Drugs like Cimetidine, Famotidine, Ranitidine, Sucralfate, Prostaglandins, Omeprazole, Anticholinergics but many case studies shows that they having many major side effects likes; PPIs having higher risk of fracture (Yang X, 2006), alter iron absorption and causes iron deficiency anaemia (Sharma VR et al., 2004; Hutchinson C et al., 2007), risk of vitamine B12 deficiency.

When acid suppressive therapy is given that time higher chance of community acquired pneumonia is present. Both H\textsubscript{2} receptor antagonist and PPIs have major effect on cardiac system. It’s prolong atrioventricular conducting time, sinus arrest, sinus bradycardia and higher risk of community acquired pneumonia. (Laheij, 2004;
Gulmez, 2007; Eom S et al., 2011) New drugs Famotidine and Nizatidine shown decrease stroke volume (Halabi AV & Kirch W, 1992; Hinrichsen H et al., 1992; Kirch W et al., 1989) and also shows negative chronotropic effect (Halabi AV& Kirch W, 1991)

People can used many marketed for gastric ulcer like Cimetidine, Famotidine, Ranitidine, Sucralfate, Prostaglandins, Omeprazole, Anticholinergics but many case studies shows that they having many major side effects likes; PPIs having higher risk of fracture, alter iron absorption and causes iron deficiency anaemia (Sharma R. 2004), risk of vitamine B12 deficiency. When acid suppressive therapy is given that time higher chance of community acquired pneumonia is present. Both H2 receptor antagonist and PPIs have major effect on cardiac system it’s prolong atrioventricular conducting time, sinus arrest, sinus bradycardia.(Hinrichsen, 1992) and higher risk of community acquired pneumonia.( Gulmez , 2007) New drugs Famotidine and Nizatidine shown decrease stroke volume (Kirch W, 1989) and also shows negative chronotropic effect. The drugs used in gastric ulcer and acidity have major drug-drug interaction. few examples are given in below. The clopidigrel drug used in platelet aggregation to inhibit aggregation having contraindication when it used with proton pump inhibitors. It reduce its anti-platelet activity.(Halabi A. 1991, Gilard M, 2006)

Drugs use in peptic ulcer having less of morbidity and mortality but may create many unlikeable reactions like gynecomastia, sterility, haemopoietic variations along with that higher chances of recurrence. (Ogawa 2010)

Communicated with tribal people who are practicing with traditional medicines and from Pubmed, Science Direct, Medline, website, drug information center, standard
books, physicochemical database, Pharmacopeia, Internet facilities, literature search.

All three plant materials, viz Dalbergia sissoo, Carissa carandas and Gymnema sylverstre were collected from forest of Dharampur, Dist- Valsad, Gujarat and authenticated by Dr. S.B. Narkhede, Asso. Prof Department of Pharmacognosy. Specimens of above plants were placed in herbarium of Smt. BNB Swaminrayan Pharmacy College, Salvav (PCOG.H-221).

The powdered material was subjected to solvent extraction using polar and non-polar solvents. Three different kind of solvent were used; petroleum ether, chloroform, alcohol, aqueous for each selected plants.

These above extracts have been exposed to Phytochemical investigations to recognize phytoconstituent present. Alcoholic bark extract of Dalbergia sissoo containing carbohydrates, amino acid, proteins, phenolic compounds and flavonoids. Alcoholic bark extract of Gymnema sylverstre contain tannin, flavonoids, triterpenoids, sapponins, and alkaloids. Alcoholic root extract contains carbohydrates, tannin, steroids, phytosterol, flavonoids, triterpenoids, saponins.

It has been carried out as per OECD guidelines and LD50 was determined and as per CPCSEA guideline therapeutic dose was calculated for different experimental animal models. In case of Dalbergia sissoo extract and Carissa carandas extract 500mg/kg and for Gymnema sylverstre extract 200 mg/kg dose get fixed.

This activity was assessed by using following model Acetic acid induces chronic gastric ulcer, Pylorus ligated rats and Stress induced gastric ulcer. Out of all extracts alcoholic extract of each selected drugs were showed more potent anti ulcer activity and after that using selected particular extract we make formulation of them. Evaluation and stability studies of formulations were carried out. Hyphenated
analytical techniques were used for analysis of complex mixtures of natural origin. After completing experiments results was obtained.

The factual importance was evaluated utilizing restricted investigation of fluctuation (ANOVA) test for Stastical analysis. For looking at nonparametric ulcer scores, ANOVA took after by Tukey-Kramer test will utilize. qualities will be express as mean + S.E.M and level of importance will be figured.

In last few decades global visions of medicines get changed. Worldwide researchers look forward to herbal medicine. They are believed that traditional herbal medicine may carry potency and safe. (Tandon and Goel 2004) The globally medical herbology get accepted. The term medical herbology is study of plants or herbs for medicinal purpose. In broadly it is said to be cultivation, collection and dispensing of herb used in medical purpose. Medical herbology also be known as a herbal medicine, botanical medicine, phytotherapy.(Ameh 2010) It was more noted that plants formed secondary metabolite in metabolic activity with respond to ecophysiological stimuli. These secondary metabolites like alkaloids, terpenes, steroids ect. are called phytochemicals which are used to treat many disease in humans. World Health Organization also shows their interest in phytochemicals by giving place in their regulations. (WHO, 1998a) The guideline on quality control of tredicinal drug, had been framed for worldwide regulation of herbal medicine. lants having heavy metal, toxins, microbial contamination under limit of WHO. The phytochemicals present in plants are easily separated by TLC and HPLC technique. The plants come in medicine having constant and repeatedly give values of loss on dryingwater extractability and ash vaue of herbal molecules. The plants having no threat of their active molecules or any adverse effects.
The phytochemicals obtain from plants are safe in animals. Herbal drugs globally with their Regulatory status: To fulfil primary healthcare need majority of population depends on traditional medicine, its about 80% and 90% which is not regulated by government. In 1999 people of developing countries are depend on traditional medicine was 80% but they contributed only 7.2% to trade. But people of developed countries relies less and contribute 55.2%. Asian countries contribute 37.6%. (Ameh 2010) This happened because of developed nation formulate traditional medicine with GMP and used it with GCP.

Not in India but in china and Korea also kept traditional medicine into national health scheme. Traditional medicine having same as it given to synthetic medicine. In china 1249 traditional medicine took as an essential medicine in 2001 with sales in billion dollars. Herbal remedies also need authority for marketing as per state drug administration law comes under 1985 in china.

In India most commanding approaches towards herbal medicine. All approaches about herbal drugs for all diseases given in Ayurveda. Vedas and Samhitas also had given ideas about same. Ayurvedic medicine is recognised by Indian Medicine Council Act 1970. WHO also took interest and give funds to encourage research in herbal medicine and in Ayurvedic medicine. Many plants having variety of therapeutic action so it can use in various diseases. Majorly we can find anti oxidant action in plants. Phenol, aromatic amines are majorly found as a phytochemical in plants. Phytochemicals can act differently at different stages generally it having ability to reduce oxygen concentration, reduce superoxide formation, lipid peroxidation, etc. Plants acquired large variety of therapeutic action but in very less amount of thorough study took place on it. Clinical study proved that many plants
having ability to treat gastric disorders. Research on it may un-covered mechanism behind it.(Gurbuz, 2007)

Herbal medicine, a good and alternative therapy of Ulcer: Stephen Defelice gave term NUTRACEUTICAL in 1989 which was used as nutrition and pharmaceutical which describe as a food or any nutrient rich substance used in inhibition, identification and cure of diseases.(Toniolo L. 2001) Recently many research were carried out on nutrition reached plants and their phytochemicals. They concluded that near about 90% of disease can avoidable if we change in our dietary habits. (Swanson 1998, Brower 1998) Because of such a powerful result of herbal component and phytochemicals it increase consumer awareness and potential benefits of substance get by plants in health related problems. So more research has been done on herbal medicine for different diseases.(Block G. 1992, Trichopoulos D. 1996) Where as many herbal plants get used in preparation of nontoxic, less expensive and easily available drugs for treatment of many disorders including gastric ulcer.
5.2. Conclusion:

All approaches about herbal drugs for all diseases given in Ayurveda. Vedas and Samhitas also had given ideas about same. Ayurvedic medicine is recognised by Indian Medicine Council Act 1970. WHO also took interest and give funds to encourage research in herbal medicine and in Ayurvedic medicine. Many plants having variety of therapeutic action so it can use in various diseases. Majorly we can find anti oxidant action in plants. Phenol, aromatic amines are majorly found as a phytochemical in plants. Phytochemicals can act differently at different stages generally it having ability to reduce oxygen concentration, reduce superoxide formation, lipid peroxidation, etc. Plants acquired large variety of therapeutic action but in very less amount of thorough study took place on it.

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From above experiment we concluded that all extracts of *Dalbergia sissoo*, *Carissa carandas*, *Gymnema sylverstre* and all the formulation made using these extracts having significant anti ulcer activity in chronic and acute gastric ulcer model but out of that alcoholic extract and formulation A was more potent.

### 5.3. Recommendations:

The Research work can be extended:

- Further, more herbal extracts can be screened for its Anti- ulcer Activity and used for treatment.

- Anti- ulcer activity should be evaluated of Polyherabal formulation for its synergistic action.

- Clinical Trials of Polyherbal formulations should be carried out for Anti- ulcer activity.
5.4. Future Scope of Research Work:

✓ Present study mainly focused on using natural resources in greater amount both from toxicity as well as cost oriented issues.

✓ Natural components are easily obtainable. Hence, in future it can effectively replace synthetic derivatives.

✓ Benefits are like free from toxicity, needed in little quantity plus effortlessly obtainable at fewer prices in contrast to synthetic component to achieve higher yield, optimization as well as novel processes serve such purpose by providing optimal criteria to conduct experiments. Such issues should be focus in near future.

✓ The all three plants were found having activity against GI Ulcers as evident from this study.
Pharmacologic activities which may be a hint to investigate use of herbal as therapeutic agents.

Hence, This may be useful to discover safer substitute for Ulcer management for numerous ailments.

However, Future work can be done for isolating its main constituents which are responsible for this activity and for elucidating its mechanism of action of Anti- ulcer activity of these three plant extracts.
5.5. Limitations of Research Work:

✓ In Herbal formulation, extraction is the foremost vital step in plant study since grounding of basic extracts commencing foliage is preliminary peak to partition as well as to decontaminate components there in flora.

✓ Medical plant investigation is intended at seclusion and recognition of obviously happening constituents. Greater part of mining action for fortitude of plant substances is urbanized in a mode so as to finishing whole introduced hooked on GC and HPLC have only elements with all interferences detached. This is single district wherever customary techniques have sounded absolute hardship. Conformist techniques for taking out of vigorous substances are point in time as well as solvent overriding, thermally precarious plus examination of abundant components in natural stuff is partial through pulling out pace.