2. Review of Literature

2.1 Infectious diseases:

Infectious diseases are deadly and the second leading cause of death worldwide (WHO, 1999). According to the report by WHO, (1999) (Figure 2.1), out of 53.9 million of deaths in 1998, 31 % was due to the cardiovascular diseases, 25 % by infectious diseases, 13 % by various types of cancers, 11 % by injuries, 9 % by respiratory and digestive diseases and the remaining 11 % were due to the maternal and other diseases. Due to the continual emergence (diseases not been previously identified) and re-emergence (diseases which have appeared in a more virulent form) of the diseases, there is a global impact on particularly the infectious diseases which will always be on the rise and a concern for a major health issue world-wide.

![Leading causes of death](image)

Figure 2.1: Infectious diseases: second leading cause of death (Source:WHO, 1999)

2.1.1 Pathogenic infections and chronic diseases:
In the latter half of 20th century, pathogenic strains have been reported to be involved with chronic diseases (Figure 2.2) like most of the peptic ulcer and gastric cancer are due to the *Helicobacter pylori* infection (37%). Other cancers like, cervical cancer, anal and vulvar carcinoma are because of the infection by human papilloma virus (27.90%). Hepatitis B and C virus infection may cause hepatocellular cancer (24.80%). Burkitt’s lymphoma and nasopharyngeal cancer are a result from the infection due to the Epstein-Barr virus (10.30%). The results are alarming showing a high rate of almost 18.6% of all the cancers is directly or indirectly associated with the infections emerging from various pathogens including bacteria, viruses and parasites (Hausen, 2009).

![Cancer due to infections](image)

**Figure 2.2: Estimated global cancer rate due to infections (Source: Hausen, 2009)**

Other pathogenic infections which lead to chronic diseases are: Kaposi’s sarcoma due to the infection made by human herpes virus 8; T cell leukemia caused due to the infection induced by human T lymphotrophic virus type 1; lyme arthritis disease due to *Borrelia burgdorferi* infection; Whipple’s disease due to the infection by *Tropheryma whippelii* (Relman, 1999; Cassell, 1998; Lorber, 1996).

### 2.1.2 Multi drug resistant microorganisms:

The microbial resistance acquired by the microorganisms against the antibiotics has been a serious problem and the situation worsened because of the widespread of the
infections, overuse and inappropriate usage of the antibiotics (Levy, 1998). Due to the frequent usage of the antibiotics, the bacteria are able to acquire and adapt themselves to develop resistance. The resistant bacteria multiply and transfer its resistant genes by plasmid exchange resulting into the advent of multi-drug resistant infection by various pathogens. The microbial resistance depends on factors like, antibiotic dosage, concentration and their time of treatment etc. (Coates et al., 2002).

Sibanda and Okoh, (2007) have reported that most of the clinical isolate strains of various pathogens are found to be resistant including Staphylococcus aureus, Staphylococcus pyrogenes and Mycobacterium tuberculosis. Many other pathogenic strains have also been reported as multi-drug resistant like Streptococcus pneumonia (Albrich et al., 2004), Helicobacter pylori (Torres et al., 2001), Haemophilus influenzae (Pfeifer et al., 2013), Pseudomonas aeruginosa (Aloush et al., 2006), Vibrio cholerae (Roy et al., 2012), Escherichia coli (Tadesse et al., 2012), Klebsiella pneumonia (Ktari et al., 2006) etc. Thus, it has been seen that multi-drug resistance has been exhibited by most of the infectious strains till now.

2.2 Helicobacter pylori - bacteria and infection:

Helicobacter pylori (gram negative) is a microaerophilic bacterial helical that inhabits in the various areas of the stomach and duodenum resulting into gastritis, peptic ulcer and gastric cancer. It is lophotrichous and highly motile with multi-polar flagella (Berry and Sagar, 2006; Covacci et al., 1999).

H. pylori manages to live for decades in the extreme acidic condition of the human stomach. Since, the bacterium is capable of producing urease (enzyme) it breaks down urea to ammonia and carbon dioxide, decreasing the acidity of the stomach and thereby able to make the environment neutral and suitable for its survival and multiplication (Eaton et al., 1991).

The H. pylori infection usually occurs within a few weeks of primary exposure. After the initial exposure, many biochemical and immunological reactions takes place inside the body which leads to the initial onset, progress and development of the disease depending upon the severity of the infection acquired. Colonisation of H. pylori is usually for life long and may lead to chronic gastritis (low level inflammation of the stomach lining), duodenal and gastric ulcer and finally gastric
cancer. Since, the discovery of *H. pylori* bacterium in 1984 by Marshall and Warren, it has been recognised as the major cause of peptic ulcer disease and an important factor leading to gastric cancer leaving stress and socio-economic factors behind which were earlier considered to be the main factors prior to the *H. pylori* discovery (Covacci *et al.*, 1999).

### 2.2.1 Epidemiology of *H. pylori* infection:

Today *H. pylori* have been successfully able to infect the upper gastrointestinal tract of almost 50% of the current world population and over 80% of the individual out of them are found to be asymptomatic (Atherton, 2006). *H. pylori* is also associated with the gastric adenocarcinoma and the mucosa associated lymphoid tissue (MALT) (Berry and Sagar, 2006). Each year atleast 7 million cases of gastric and duodenal ulcers, adenocarcinoma and MALT lymphoma occur worldwide resulting in large number of deaths (Covacci *et al.*, 1999).

The extent of *H. pylori* infection varies due to the various factors involved and it is usually seen that in most developed countries it is on a decline (Brown, 2000). The primary acquisition of the *H. pylori* infection in the adults and the occurrence of re-infection after successful eradication are usually low with an annual incidence of only 0.3-0.7 % and 6-14 % in the developed and the developing countries respectively. Also it has been noted that the *H. pylori* infection is more prevalent in males with almost 20-30% higher rates than in the females of many populations (Covacci *et al.*, 1999).

### 2.2.2 Mode of transmission:

Till now there are uncertainties on how the *H. pylori* infection is usually encountered and its mode of transmission still remains a mystery. Many reports have shown that humans are the only present reservoir of the *H. pylori* infection (Hannula and Hanninen, 2007) thus, it is more likely that the *H. pylori* infection is transmitted through various family members including siblings, parents and children through the gastro-oral route as human contact continues to be one of the major mode for its
transmission. *H. pylori* infection is a hazardous tool for the performing gastroenterologists who usually come in contact with the bacteria while doing endoscopy and may lead to the transmission of the infection due to the improper cleaning and repeated use of the same endoscopy tool if used without sterilization.

### 2.2.3 *H. pylori* a chronic infection, virulence and pathogenesis:

*H. pylori* infection usually persists for life if remained untreated and it is seen that multiple *H. pylori* infections (from different strains of the same bacterium) do coexist specially in the developing countries. DNA is very easily exchanged between strains which allow the bacterium to spread the genes among various strains encoding major virulence factors including the antibiotic resistance (Graham, 1997). *H. pylori* infection causes almost a two-fold increase in the risk of developing gastric cancer particularly in strains expressing the cytotoxin-associated gene A antigen, Cag A (Enroth et al., 2000).

Many factors account for its virulence which makes it able to survive, colonize and establish infection. The important ones are the presence of urease, flagella, shape and the adhesins.

#### 2.2.3.1 Urease enzyme:

The production of urease enzyme by *H. pylori* makes it well adapted to survive and establish itself in the gastric mucosa. The urease breaks urea to ammonia when *H. pylori* infection occurs in the stomach. The formation of ammonia ions neutralizes the gastric juice (acidic) and thus, the *H. pylori* are able to adapt, survive and establish itself in extreme acidic conditions (Eaton et al., 1991).

Urease enzyme is also produced by several other microorganisms apart from *H. pylori* like *Proteus mirabilis, Staphylococcus saprophyticus, Yersinia enterocolitica*, etc. The urease molecule differs in size and structure among the microorganisms. The *H. pylori* urease molecule is usually larger in size with molecular weight > 300 kDa and has a smaller most active subunit called Urease B (Mobley et al., 2001).

#### 2.2.3.2 Flagella:

Flagella help the bacteria for motility through the viscous gastric mucus. They enable them to reach to a place (below the mucus) where the pH is neutral and the
bacteria are able to inhabit easily (Eaton and Krakowka, 1994). The flagella are unipolar with two to six sheaths. They are mainly composed of co-polymerized flagellins, fla A and fla B. The mucin layer of the flagella is composed of multi polysaccharides. The sheath of the flagella is also known to play a key role in protecting the bacterium from the acidic environment of the stomach (Spohn and Scarlato, 1999).

2.2.3.3 Shape:

The *H. pylori* bacteria are helix in shape. They are more or less also s-shaped which enables a smooth movement of the bacteria through the viscous mucin (Slomiany *et al.*, 1992). Due to its unique shape and motility the *H. pylori* bacteria are able to survive and multiply in the gastric mucosa unlike the various other bacteria. Researchers have discovered a group of four proteins which are coiled-coil-rich-proteins (Ccrp) which have known to play a key role in the shape of *H. pylori*. Ccrp proteins are responsible for the extended filamentous structures and they essentially account for the typical cell morphology (Specht *et al.*, 2011). Some mutant forms of *H. pylori* which lack these specific proteins are unable to colonize in the stomach lining.

2.2.3.4 Adhesins:

*H. pylori* moves actively towards high concentration areas of urea and bicarbonate in the mucosa of the host where it comes in contact with the mucin layer which leads to adherence between the mucin layer of the host and the *H. pylori* (Yoshiyama *et al.*, 1999). *H. pylori* contain many types of adhesins like, sialic acid sulphated and lapidated compounds. The adhesins mediate interaction between *H. pylori* and the host cell surface. Three genes (hpaA, nap and sapA) out of six accounting for the sialic acid adhesin have been identified till now (Testerman *et al.*, 2001). Bab A adhesin is the fourth adhesin which particularly binds to Lewis B (LeB) antigen in mucin MUC5AC (Azevedo *et al.*, 2008). It is reported by many researchers that sialic acid adhesins varies from strain to strain and not all *H. pylori* strains show the presence of these adhesins.

2.2.4 Diagnosis of *H. pylori*:
*H. pylori* diagnosis is usually suggested after symptoms are seen for a possible infection. Many gastro-duodenal diseases are linked to *H. pylori* infection. Though many tests have been proposed for detecting the infection, however, none of the detection methods are completely safe. Diagnosis of *H. pylori* can be divided into two types of test: Invasive tests and Non-invasive tests.

### 2.2.4.1 Invasive tests:

Many invasive tests are into practise for the early detection of *H. pylori* infection. Methods used are histological diagnosis of endoscopic biopsy, culture investigation and rapid urease tests with their specific benefits and defects (Tanih *et al.*, 2008). Since, the infection is usually patchy, the biopsy based methods are highly prone to sampling errors. To avoid report error, usually multiple biopsies are performed (both antrum and corpus) and also other invasive tests are done to ensure and confirm the test result.

#### 2.2.4.1.1 Histology:

Histology is capable of revealing the presence of the bacteria and also the type of inflammation. *H. pylori* infection is usually identified by the haematoxylin and the eosin stain. Some stains like, Genta, Gimenez, Giemsa, Creosyl violet, Wartgin-Starry silver are used for the morphological identification and to detect the infection (low levels) (Ndip *et al.*, 2003). The Giemsa stain is the most preferred stain due to its simplicity, sensitivity and reduced cost (Gatta *et al.*, 2003). Advantage of doing histology is that apart from the histological information provided, the biopsy sections can also be screened for gastritis, atrophy and intestinal metaplasia.

#### 2.2.4.1.2 Culture:

Microbial isolation of the culture samples might be unreliable due to slow growing nature and frequent contamination. Culture detection is regarded as the least sensitive method of detection (Megraud and Lehours, 2007) and identification of the cultured bacteria is usually carried out by the presence of various enzymes like,
catalase, cytochrome oxidase, \( \gamma \)-glutamyl transpeptidase, urease, alkaline phosphatase and leucine aminopeptidase (Tanih et al., 2008).

2.2.4.1.3 Rapid urease test (RUT):

RUT is a diagnostic technique which is fast, simple and used for the immediate detection of infection in the body. It is regarded as a benchmark test for the detection of \( H. \) pylori infection. Since, it is a rapid test, the results are usually obtained within 90 min and thus, it helps in treating the patients on time. The test is highly sensitive as the entire biopsy sample is placed on the media which leads to less sampling and additional processing error. The presence of \( H. \) pylori allows the urease to break the urea, increase the pH leading to a colour change from yellow to red (Berry and Sagar, 2006).

2.2.4.2 Non-invasive tests:

Non-invasive tests are tests which are based on the serological analysis, urea breath test and the faecal antigen test. The serological test involves the blood analysis, the faecal antigen test involves the stool sample investigation and the urea breath test involves the breath sample analysis.

2.2.4.2.1 Serology:

This test is based on the detection of the antibody response. The IgG antibody to the \( H. \) pylori is detected by ELISA or the latex agglutination tests. This detection method is usually simple, reproducible and affordable which can also be performed on stored samples. There is a variation in the antibody responses to the \( H. \) pylori antigens among individuals. The serological detection method involves only a general finger prick test that comprises of a fixed and a solid phase assay using polystyrene bead coated with \( H. \) pylori antigen which detects the presence of \( H. \) pylori immunoglobulins by chemiluminiscent enzyme technique (Logan et al., 1991).

2.2.4.2.2 Urea breath test:

In urea breath test, the patient is made to drink \( ^{13} \)C labelled urea which gets rapidly hydrolyzed into \( CO_2 \) by the urease enzyme of the bacterium which is then, absorbed into the gastric mucosa and finally excreted as carbon dioxide (labelled) and then
detected in the expired breath. The test is simple and can be easily used to detect the current infection and also to assess the eradication after treatment (Logan et al., 1991).

2.2.4.2.3 Faecal antigen test:

The faecal antigen or the stool antigen test usually gives good result in children. This test is based on the sandwich ELISA method and is used detect the presence of the \textit{H. pylori} antigens present in the stool. The test seems to be less expensive. The method involves the use of polyclonal antibodies to \textit{H. pylori} which gets adsorbed in the micro wells. When \textit{H. pylori} present in the faecal samples of the patient are added to the well, they get attached to the adsorbed antibody. When \textit{H. pylori} antibody attached with the peroxidase is added again, they get bind to the \textit{H. pylori}. The unbound material gets washes away and the substrate then, reacts to the attached peroxidase enzyme which produces a colour, greater the intensity of the colour, more is the \textit{H. pylori} content (Gisbert and Pajares, 2004).

2.2.5 Treatment against \textit{H. pylori} infection:

Many drug treatment regimens have been used against the \textit{H. pylori} infection. The standard treatment regimen is a triple therapy involving two antibiotics and a proton pump inhibitor. Commonly used antibiotics are metronidazole, amoxicillin, clarithromycin and proton pump inhibitor is omeprazole (Malfertheiner et al., 2007). This treatment however, is not successful every time since the bacteria acquires resistance easily. Additional quadruple therapy involves the usage of a bismuth colloid (Stenstrom et al., 2008).

Eradiation of this bacterium is not always successful mainly due to the acquisition of multidrug resistance which is a cause of major concern with many other pathogenic strains as well and thereby, leads to inefficient treatment efficacy (De et al., 2009). Due to the incomplete cure achieved by the present treatment therapy, undesirable side effects (nausea, vomit, gastric pain, diarrhoea, abdominal discomfort), non-compliance among the patients, misuse of the antibiotics and high cost involved in the treatment, there is an urgent need for the development of new treatment strategies to combat this deadly pathogen (Broutet et al., 2003; Wong et al., 2003; Myllyluoma et al., 2005).
Combination therapy in the treatment of *H. pylori* infection has generated a considerable interest in the study of medicinal plants as potential source of new drugs against the treatment of this pathogenic organism. The high complexity of the bioactive compounds from plants coupled with their broad antimicrobial activity may make it difficult for the pathogenic organisms, including *H. pylori* to acquire resistance during treatment (Cowan, 1999).

### 2.3 Plants: A source of antimicrobial, antioxidant and various bioactive compounds:

There has been a growing interest in the phytochemical approach for the eradication of this bacterium, mainly due to the decline in the efficacy of the currently used drugs, most of which have either failed or turned out to be ineffective. The combination of antibacterial and antioxidant activity is an ideal way of treating the various infections caused by the pathogenic strains and antioxidants are known to play an important role in the gastro duodenal mucosal inflammation, peptic ulcer disease and against gastric cancer (Nair *et al.*, 2000).

Moreover, Zhang *et al.*, (1997) have shown multiple functions of vitamin-C as antioxidant, free radical scavenger and also as a good antimicrobial compound (*in-vitro* and *in-vivo*).
When vitamin-C is taken orally by an individual, ascorbic acid gets oxidized to dehydroascorbic acid (DHA). DHA is absorbed by the small intestine, and then is reduced back to ascorbic acid by the blood cells. From the blood, it is secreted into the stomach and finally eliminated through urine (Akyon, 2002).

The medicinal and pharmacological properties of the medicinal plants have been a subject to numerous investigations (biological and pharmacological) with interesting results. Based on the available literature, some of the Indian medicinal plants were therefore selected for both antibacterial and antioxidant studies.

2.3.1 Bacopa monnieri:

*Bacopa monnieri* or brahmi is used since ancient times in ayurveda because of its multiple properties. One of the main properties of the plant is its use as memory enhancer, good for the brain as an active ingredient of many nerve tonics. The plant has been effective as a sedative and tranquiliser. Several studies have also shown the plant being used as an anti-depressant, anti-anxiety, anti-epileptic, antioxidant, adaptogenic, protective effects against the DNA damage and gastrointestinal ulcer etc. (Gohil and Patel, 2010).

2.3.1.1 Compounds isolated from *Bacopa monnieri*:

A number of active compounds have been reported from *B. monnieri*. Phytochemicals like, alkaloids (brahmine, nicotine, herpestine), saponins (hersaponin and potassium salts), sterols, D-mannitol. The major compound bacoside A is responsible for the neuropharmacological effects. Bacoside A generally co-occurs and exists with bacoside B differing only in the optical rotation. During the acid hydrolysis of the bacosides, two sapogenins (jujubogenin and pseudojujubogenin), a mixture of aglycones (bacogenin A1, A2 and A3) and bacogenin A4 (ebelin lactone pseudojujubogenin) are formed. Four new triterpenoid saponins (bacopasaponins A, B, C and D) were also reported to be present in the plant. The glycosidic methanolic fraction has also reported the presence of bacopaside I and II. Later three new phenylethnoid glycosides (monnierasides I- III) and three new saponins, bacopasides III-V were isolated from *B. monnieri*. A new
glycoside (phenylethyl alcohol) and Bacopasaponin G (jujubogenin) were also isolated (Gohil and Patel, 2010).

2.3.2 Ocimum tenuiflorum:

It is also known as holy basil or tulsi. It is an aromatic, sacred, grassy and annual plant from the Lamiaceae family. It is grown for religious purposes and medicinal qualities. Its main phytocomponent is the essential oil. The plant has been used traditionally as a medicinal herb in the treatment against headache, cough, diarrhoea, constipation, warts, worms, as an adaptogen, against kidney disorders and various infectious diseases caused by pathogens (*P. aeruginosa*, *S. aureus* and *E. coli*) (Mishra and Mishra, 2011).

2.3.2.1 Compounds isolated from Ocimum tenuiflorum:

The beneficial effects of the plant are a result of the presence of various secondary metabolites. The plant contains phytochemicals like, alkaloids, steroids, tannins, phenolics, flavonoids, anthocyanins, steroids, resins, fatty acids, gum etc. It is also a source of numerous aromatic compounds and essential oils. The presence of the phenolics and flavonoids makes it a potent antioxidant, free radical scavenger and metal chelator (Mishra and Mishra, 2011). Some of the main constituents of *O. tenuiflorum* are germacrene D, ursolic acid, eugenol, oleanolic acid, carvacrol, rosmarinic acid, ß- elemene, linalool and ß- caryophyllene, (Padalia and Verma, 2011).

2.3.3 Azadirachta indica:

It is also known as neem is an evergreen plant of the Meliaceae family. It is a potent medicinal plant with multiple biological activities of its various parts against many pathogenic strains like, *Bacillus cereus*, *Escherichia coli*, *Streptococcus mutans*, *Lactobacillus* sp., *Streptococcus faecalis*, *Klebsiella pneumonia*, *Helicobacter pylori* and many more. The different extracts of the plant have reported to possess antibacterial activities, antiviral and antifungal properties (Atawodi and Atawodi, 2009). A study by Bandhopadhyay *et al.*, (2004) has shown the comparision of the *A. indica* extract with the known antiulcer drugs, ranitidine and omeprazole in the
pyloric ligation and the stress ulcer models, the *A. indica* extract was found to be almost equivalent to the standard drugs.

2.3.3.1 Compounds isolated from *Azadirachta indica*:

Greater than 135 bioactive compounds have been isolated from the various parts of *A. indica* (Girish and Shankara, 2008). Some of the isolated compounds present in *A. indica* extracts are limonoids (diterpenoids, triterpenoids containing protomeliacins, mahmoodin), tetrantortriterpenoids (azadirone, epoxyazadiradione, genudin and its derivatives), secomeliacins (azadirachtin, salannin, nimbin, azadiradione, deacetylnimbin, 17-hydroxyazadirdione and protolimonoid, naheedin) and vilarin. Nimbin was the first one to be isolated and studied and azadirachtin is one of the most important bioactive compounds of *A. indica*. The plant was also found to contain the non-isoprenoids like, sulphurous compounds, carbohydrates and amino acids, and polyphenolics such as coumarin, dihydrochalcone, flavonoids and their glycosides, phenolic acids, aliphatic compounds and tannins (Atawodi and Atawodi, 2009).

2.3.4 *Aloe vera*:

It is a succulent plant from the Liliaceal family. It has the ability to survive in harsh environmental conditions. The plant possesses wound healing, anti-inflammatory, immunomodulatory, anti/protozoal, burn healing, UV protective and antibiotic effects (Palanikumar and Panneerselvam, 2010). It is a known herbal drug also used in the cosmetic industry for its cooling effects. It has been reported to be used against diseases like, cancer, ulcers, diabetes, against hepatotoxic effect, inflammation, oxidative stress and also used as anti-leishmanial, antifungal, antiviral etc. (Megraj et al., 2011). According to Kumari *et al.*, (2010) there are only few studies till now which have demonstrated the antimicrobial activity of *A. vera* against *H. pylori* strains.

2.3.4.1 Compounds isolated from *Aloe vera*:

The plant contains several potential bioactive compounds. Glycoproteins, anthraquinones (aloin, aloetic acid, aloe-emodin, barbaloin, anthranol, emodin, isobarbaloin,), saccharides (cellulose, aldopentose, mannose, glucose, glucomannan, acetylated mannann, glucogalactomannan, acetylated glucomannan,
galactogalacturan, galactoglucoarabinomannan, galactose and galacturonic acid), low molecular weight substances (arachidonic acid, cholesterol, gibberellins, salicylic acid, lignins, aloesin, uric acid, triglycerides, steroids, β-sitosterol, diethylhexylphthalate), vitamins (B1, B2, α-tocopherol, folic acid, choline, C, B6, B2, β-carotene and B1), enzymes (oxidase, carboxypeptidase, lipase, cyclooxygenase, catalase, amylase) are the known compounds (Palanikumar and Panneerselvam, 2010).

2.3.5 Fumaria parviflora:

*Fumaria parviflora* is a flowering and weedy plant which belongs to the family of Fumaraceae. It was not reported to show anti-*H. pylori* activity. It is found to be hepatoprotective against nimesulide hepatotoxicity (Tripathi et al., 2010). *F. parviflora* has been known to be an important ingredient of mouthwash as it is useful in reducing gums inflammation (Abdeirahman et al., 2002). According to Vahabhi et al., (2011) no report on antimicrobial activity of *F. parviflora* has been found. However, Parekh and Chanda, (2007) have evaluated the antibacterial activity of *Fumaria indica* (aqueous and ethanolic) extracts against some selected members of Enterobacteriaceae. It also possesses acetylcholinesterase inhibitor activity, hepatoprotective, antinoceptive, antioxidant, antihelmintic and analgesic activity (Kaur et al., 2012).

2.3.5.1 Compounds isolated from *Fumaria parviflora*:

Not many compounds have been isolated from the plant. However, the reported phytochemicals in *F. parviflora* are alkaloids, flavonoids, glycosides, saponins, steroids, triterpenoids, tannins, sugar and potassium salt (Kaur et al., 2012; Rao et al., 2007). Some of the main alkaloids of *F. parviflora* are protopine, fumarizine, papraine, papracine papracinine, paprafumicine and papraraine (Al-Shaibani et al., 2009).

2.3.6 Mentha arvensis:

*Mentha arvensis* or mint belongs to the Lamiaceae family. It is an erect branched aromatic perennial herb. It is used as an antispasmodic, carminative, anti-peptic ulcer agent, against indigestion, skin ailments, cough and cold. The plant is also effective against liver and spleen ailments, asthma, and jaundice. The oil (90%) of the plant
is known to be antiseptic, refrigerant, stimulant and diuretic and effective against rheumatic pains (Londonkar and Poddar, 2009; Nair and Chanda, 2007).

2.3.6.1 Compounds isolated from Mentha arvensis:

Some of the known compounds of M. arvensis are monoterpenes (limonene, methyl acetate cineole, menthofuran and menthone), sesquiterpenes (viridiflorol), flavonoids (luteolin, menthoxide, and hesperidin, rutin, isorhoifolin, menthoxide and luteolin), phenolic acids (rosmarinic acid, chlorogenic acid and caffeic acid), triterpenes (squalene, sitosterol, urosolic acid, α-amyrin and squalene), betaine, choline, carotenoids, tocopherols, phytol, cyclones, tannins and minerals (Pino, 1996; Buneton, 1995; Liest, 1998).

2.3.7 Rosa indica:

*Rosa indica* is a perennial plant belonging to the Rosaceae family. They are erect shrubs with stems having sharp thorns. The flowers are known to give fragrance (Sahoo et al., 2011; Pandey et al., 2012). The leaves and petals of the plant are good against fever, diuretic, bronchial congestion, cold and sore throat. The *R. indica* water is effective against eye irritation. The oil of the plant is effective against skin irritation and can be used for moisturizing the skin (Sahoo et al., 2011).

There are no reports on the antibacterial activity of *R. indica* petals and leaves against the *H. pylori* strains and very few reports have been found against the other bacterial pathogens (Sahoo et al., 2011). However, Koday et al., (2010) have mentioned about antibacterial activity of *R. indica* petals. *Rosa* plant extracts have been reported to show antimicrobial activity against plant pathogen like *Xanthomonas axonopodis* (Basim et al., 2003) and human pathogens like *Staphylococcus aureus, Escherichia coli, Salmonella, Bacillus cereus* (Kamijo et al., 2008).

2.3.7.1 Compounds isolated from Rosa indica:

Razungles et al., (1989) have reported the fruit extracts of two *Rosa* species (*Rosa canina* and *Rosa rugosa*) contains three carotenes (β-carotene, δ-carotene and lycopene) and six xanthophylls (β-cryptoxanthin, lutein, 5,6-epoxylutein, cis-violaxan-thin, trans-violaxanthin, neoxanthin ). Also *Rosa* hips contain the largest
amount of total carotenoids which are mainly comprised of β-carotene and lycopene. Dobson et al., (1987) have reported the presence of aliphatics, terpenoids and aromatics in the flower and pollen of *R. canina* and *R. rugosa* species.

2.3.8 *Emblica officinalis*:

*Emblica officinalis* or amla belongs to the family Euphorbiaceae. The fruits are globular and fleshy with seed in it. The fruit of the plant is a super rich source of vitamin C. It is useful as an digestive medicine, hair tonic, anti-inflammatory, antipyretic, stomachic, refrigerant, liver tonic, laxative, diuretic, cardiac tonic, astringent, against anaemia, hyperacidity, diarrhoea, eye inflammation, jaundice, wound healing, memory enhancing, lowering cholesterol levels, leucorrhea, liver disorders, cough, peptic ulcer, dyspepsia, hepatoprotective, antioxidant, oxidative stress, cardio protective, antimutagenic, cytoprotective, antitumor, antifungal, antimicrobial etc. (Majeed et al., 2009). Numerous beneficial biological properties makes it an important plant for herbal drugs.

2.3.8.1 Compounds isolated from *Emblica officinalis*:

Many researchers have indicated *E. officinalis* as the super rich source of natural ascorbic acid. The fruits of the plant also contain other phytochemicals like, carbohydrates, amino acids, phenolic compounds, alkaloids, 3-ethylgallic acid, 1,6-di-O-galloyl-β-D-glucose, corilagin, chebulagic acid, quercetin, chebulinic acid, 3,6-di-O-galloyl-D-glucose, 1-O-galloyl-β- D-glucose, ellagic acid, methyl gallate, gallic acid, isostrictinin, flavonoids (kaempferol-3-O-α, kaempferol-3-O-α-L- rhamnopyranoside,), acylated apigenin glucoside (hydrolyzable tannins, pectin, trigallayl glucose, ellagotannin, citric acid, apigenin-7-O-6”-butyryl-β- glucopyranoside, emblicanin A, emblicanin B, pedunculagin and punigluconin. The presence of all these phytochemicals has implicated its role as a potent antioxidant (Ghosal et al., 1996; Khan, 2009).

2.3.9 *Camellia sinensis* assamica:

*Camellia sinensis* is also known as tea plant and it is the most widely consumed beverage worldwide for its aroma, flavour and its physiological effects (Zhu et al., 2002). Many researchers have reported the health benefits of consuming tea like, anti-cancerous, anti-inflammatory, anti-arthritic, antibacterial, anti-angiogenic,
antiviral, neuroprotective, antioxidative (free radical scavenging and metal chelating abilities), cholesterol lowering effects and against cardiovascular diseases etc. (Chacko et al., 2010)

2.3.9.1 Compounds isolated from Camellia sinensis assamica:

The plant is rich in flavonols and polyphenolic (gallic acid) compounds. Flavonols attribute to almost 30% of its dry weight. It has abundant catechin and epigallocatechin-3-gallate. Alkaloids (methylxanthines) like caffeine, theobromine and theophylline are present.

Chemically it contains proteins, amino acids (theanine, leucine, valine, tyrosine, aspartic acid, serine, glycine, tryptophan, glutamic acid, arginine, threonine and lysine), carbohydrates (cellulose, pectin, and sucrose, fructose and glucose), minerals and trace elements (phosphorous, sodium, selenium, molybdenum, zinc, copper, iron, manganese, chromium, magnesium, aluminium, fluorine, potassium, nickel, strontium, cobalt and calcium), lipids (α-linolenic acid and linoleic), sterol (stigmasterol), vitamins E, C, B, aldehydes, carotenoids, chlorophyll, theophylline, caffeine, alcohol, ester, lactone and hydrocarbon (Chacko et al., 2010).

2.3.10 Bryophyllum pinnatum:

Bryophyllum pinnatum belongs to the family of Crassulaceae. The plant has a number of biological applications. It has been reported to show antimicrobial activity against Pseudomonas aeruginosa, Klebsiella pneumonia, Aspergillus niger, Candida albicans, Staphylococcus aureus and Escherichia coli. It has shown to have anti-ulcer, anti-hypertensive, anti-leishmanial, anti-helminthic, anti-cancer, anti-diabetic, anti-inflammatory, immunomodulatory, hepatoprotective, nephroprotective, anti-convulsant, antioxidant and wound healing activities activity (Afzal et al., 2012; Ghasil et al., 2011). No reports were seen showing anti-H. pylori activity of Bryophyllum.

2.3.10.1 Compounds isolated from Bryophyllum pinnatum:

Alkaloids, phenols, flavonoids (flavones, falvans, flavanones, isoflavonoids, chalcones, aurones, anthocyanidines), saponins, tannins, carotenoids, glycosides, sitosterol, anthocyanins, malic acid, quinines, tocopherol, lectins, coumarins,
phenanthrene derivatives 2-(undecenyl)-phenanthrene, 2(9-decenyl)-phenanthrene, 1-ethanaomino-7-hex-1-yne-5-one phenanthrine, diagremotianin, bufadienolides (bryophyllin A, B and C, bryophyllol, bryophollone, bryophollenone, bryophynol), isorhamnetin-3-o-α-L-1-C-4-rhamnopyranoside, 1-octane-3-o-α-L-arabinopyranosyl-1-6-glucopyranoside, protocatechuic-40-o-b-D-4-C-1-glucopyranoside, 24-epicerosterol, 24(R)-5α-stigmosta-7, 5α-stigmast-24-en-3β-ol, 25-dien-3β-ol, 25-methyl-5α-ergost-24, stigmata-5-en-3β-ol, stigmas-4,20, 23-trien-3-one, α-amyrin-β-D-glucopyranoside, n-dodecanyl-n-octadec-9-en-1-oate, n-undecanyl-n-octadec-9-en-1-oate, 18-α-Oleanane, ψ-taraxasterol, β-arnyrin acetate, kaempferol diglycoside (kapinnatoside), elements (calcium, phosphorous, sodium, potassium malate, magnesium, iron, zinc), vitamins (ascorbic acid, riboflavin, thiamine, niacin, casein hydrolysate, nicotinamide), phosphoenolpyruvate, protocatechuic acid, ferulic acid, para-coumaric acid, p-hydroxycinnamic acid, 4-hydroxybenzoic acid, 4-hydroxy-3-methoxy-cinnamic acid, caffeic acid, syringic acid, enzymes (phosphoenolpyruvate carboxykinase, phosphoenolpyruvate carboxylase, pyruvate orthophosphate dikinase, oxygenase, phosphoglycerate kinase, carbonic anhydrase, glycolate oxidase, fructosebiphosphate aldolase, DNA topoisomerase) were reported to be isolated from B. pinnatum (Afzal et al., 2012).

2.3.11 Murraya koenigii:

Murraya koenigii is also known as curry leaf which belongs to the family of Rutaceae. The green leaves of the plant are widely used in cookery. It has a characteristic aroma and added in food for giving flavour. It also has abundant medicinal value. They can be consumed raw to cure dysentery, diarrhoea and vomiting. The bark and roots of the plant are used against eruptions, poisonous animal bites and wound healing. The plant also shows nephro-protective, cardio-protective anti-helminthic, analgesic, anti-inflammatory, anti-pyretic, anti-ulcer, antioxidative, antimicrobial and anti-itching properties. It is used for the treatment against leucoderma, cancer, dental disorders, osteoporosis, blood disorders, piles. It is also used widely in cosmetic industries (Jain et al., 2012).

2.3.11.1 Compounds isolated from Murraya koenigii:

The compounds responsible for its aroma are o-phellandrene, p-elemene, p-caryophyllene and p-gurjunene. The plant also contains carbazole alkaloids in
abundance. Other compounds present in the plant are coumarins, acridine, alkaloids, lutein, tocopherol, carotene, koenimbine, koenigine, koenine, koenidine, koenimbidine, koenoline, murrayacine, murrayacinine, mukonidine, bis-mahanine, isomahanine, o-methyl mahanine, o-methyl murrayamine A, bis-pyrafoline, euchrestine B, bismurrayafoline E, mahanine, 1-formyl-3-methoxy-6-methyl carbazole, mahanimbine, isomahanimbine, murrayanol, murrayagentin, mahanimbidine, girinimbine, girinimbolin, mahanimbinol, mukonicine, marmesin-1′-o-β-D-galactopyranoside, gurjunene, murrayanine, girinimbine, murrayazoline, murrayazolinine, murrayazolidine, mukoline, mukolidine, lipids, essential oils (β-caryophyllene, limonene, g-terpinene, β-phellendrene, etc.) (Jain et al., 2012).

2.3.12 Syzygium aromaticum:

It is also known as clove and is a flower bud (aromatic) belonging to Myrtaceae family. *S. aromaticum* is reported to have anti-carcinogenic, antioxidant, anti-thrombotic, anti-fungal, anti-mutagenic, anti-inflammatory, anti-ulcerogenic, anti-parasitic and anti-arthritis activities. It is also effective against Alzheimer’s disease and lowering cholesterol level. The oil from *S. aromaticum* is used against dental disorders. It is also extensively used in the fragrance and flavouring industries (Saeed and Tariq, 2008).

2.3.12.1 Compounds isolated from *Syzygium aromaticum*:

The essential oil of *S. aromaticum* contains 44.2 % of eugenol (Ozturk and Ozbek, 2005). Eugenol is a phenolic compound and the main component present in the bud (Ali et al., 2005). Eugenol from *S. aromaticum* induces glutathione-s-transferase enzyme which plays a key role in the detoxification of liver and intestine. Zheng et al., (1992) have reported the presence of phytochemicals like eugenol, acetyleneugenol, chavicol, acetyl salicyclate and humulenes in *S. aromaticum* bud.

It has been reported that a variety of *Syzygium* species are a source of many important phytoconstituents like, polyphenols, gallic and ellagic acid derivatives, tannins and flavonol glycosides. *S. aromaticum* contains about 15-20 % essential oil, 13 % tannins, 10 % fixed oil and 6-12 % non-essential ether extract. The main components of essential oil are identified to be eugenol, eugenyl acetate and β-caryophyllene. Eugenol (4-allyl-2-methoxyphenol) constitutes almost 70-90 % by
weight, eugenol acetate (> 17 %) and cariofilen (> 12 %), β-caryophyllene (9 %), δ-cadinene (3.6 %), α-copaen (1.0 %), 1,8-cineole (0.1 %), α-humulene (3.5 %), linalool (0.2 %), β-cadinene (0.5 %), epizonarene (0.1 %), α-muurolene (0.1 %), eugenyl acetate (4.2 %). Eugenol also constitutes methoxy benzaldehyde, benzyl alcohol, benzaldehyde, carvacrol, 2-heptanone, methyl salicylate, iso-eugenol, methyl eugenol, dehydrodieugenol, phenyl propanoide, transconfireryl aldehyde, kaempferol, biflorin, oleanolic acid, gallic acid, myricetin, ellagic acid, rhamnocitrin, thymol, cinnamaldehyde, acetyl salicylate, vanillin, and crategolic acid. Apart from these phytoconstituents, *S. aromaticum* also comprises of tannins (gallotannic acid), flavonoids (eugenin, rhamnetin, and eugenitin), triterpenoids (oleanolic acid, stigmasterol and campesterol) (Singh *et al.*, 2012).

### 2.3.13 Datura metel:

*Datura metel* is also known as thorn apple / devil trumpet which belongs to Solanaceae family. It is known to show hallucinogenic activity. The plant is known for its insecticidal, herbicidal, anti-fungal, antibacterial, anti-tumorogenic, anti-inflammatory, anti-rheumatoid and anaesthetic activities. It is also effective against skin rashes, ulcers, bronchitis, jaundice, diabetes and diarrhoea, etc. (Britto and Graceline, 2011)

#### 2.3.13.1 Compounds isolated from *Datura metel*:

*D. metel* plant (fruit, buds, leaves and flower) contains phytochemical constituents like saponin, flavonoids, tannins, phenols, tropane alkaloids (hyoscyamine, daturanolone, fastusic acid, hyoscine, littorine, acetoxypompe, valtropine, fastusine, fastusinine), withanolides (baimantuoelulino C, A, B, withafastuosin E, withmetelin P, O, N, M, L, K, J, I, C), trigloyl esters of tropine and pseudotropine, glycocides, calystegines (non-tropane alkaloids), scopolamine, atropine, steroids and terpenoids (triterpene) (Akharaiyi, 2011; Monira and Munan, 2012)

Ramadan *et al.*, (2007) have characterized *D. metel* seeds extract and found that it contains a high amount of phytosterols along with stigmasterol, β-sitosterol, lanosterol, Δ5-avenasterol and sitostanol. They also reported that the major component present (80 %) was γ-tocopherol in the seed extract. The presence of numerous phytosterols in *D. metel* enhances its role as a good antioxidant.
2.4 Phytocompounds as anti-\textit{H. pylori} agents:

Medicinal plants are an abundant source of biologically active compounds, many of them have already been formulated into useful therapeutic substances or have provided a basis for the development of new and novel molecules for the pharmaceutical industry (Vitaglione and Fogliano, 2004).

Phenols, flavonoids, tannins, terpenoids, essential oils, alkaloids are some of the phytocompounds which are known to play a key role in plant defense mechanisms against the attack by plant pathogens, insects and herbivores (Cowan, 1999). These compounds have been found to exhibit antimicrobial activities against a wide range of organisms (including the multi-drug resistant strains) (Vitaglione and Fogliano, 2004). Some of the phytocompounds with anti-\textit{H. pylori} activity are discussed below.

2.4.1 Phenols and polyphenols:

Phenolic compounds are one of the important plant constituents due to their free radical scavenging activity by their hydroxyl groups (Pelczar \textit{et al.}, 1998). The phenolic compounds are known to be anti-atherogenic, anti-allergenic, anti-microbial, anti-inflammatory, antioxidant, cardioprotective, anti-thrombotic and have vasodilatory effects (Manach \textit{et al.}, 2005; Benavente \textit{et al.}, 1997; Middleton \textit{et al.}, 2000; Samman and Cook, 1998; Puupponen-Pimia \textit{et al.}, 2001).

Phenols are found in the essential oils of many plants and are proved to be active against many pathogenic bacterial strains (Suressh \textit{et al.}, 1992; Shashidhar, 2002), fungi (Shashidhar, 2002; Bilgrami \textit{et al.}, 1992) and viruses (Pacheco \textit{et al.}, 1993). Phenols have also shown their effect against \textit{H. pylori} strains (Ali \textit{et al.}, 2005).

The exact mechanism by which the phenolic compounds inhibit the growth of \textit{H. pylori} is still unknown but, reports have shown that it could be because of the inhibition of the urease activity (Lin \textit{et al.}, 2005), adhesion to the human gastric mucus (Burger \textit{et al.}, 2000), inhibition of VacA cytotoxin activity or disintegration of the outer membrane (Nohynek \textit{et al.}, 2006; Ruggiero \textit{et al.}, 2006; Yahiro \textit{et al.}, 2005).

Li \textit{et al.}, (2005) studied the effect of \textit{Syzygium aromaticum} and 29 other Chinese plants against a standard strain of \textit{H. pylori} (ATCC 43504) and 6 other clinical
isolates. The main reason for anti-*Helicobacter pylori* action of ethanol extract of *S. aromaticum* plant might be the presence of an active ingredient, eugenol which is a well characterized and important constituent of *S. aromaticum* oil.

**2.4.2 Flavonoids, flavones and flavonols:**

Flavonoids are a group of almost 4000 naturally existing phenolic compounds mostly responsible for the colour of flower and fruit (Bylka *et al*., 2004; Borrelli and Izzo, 2000). Flavonoids are an important constituent of human diet. At an average, a normal human diet contains about 1 g of flavonoids (Di Carlo *et al*., 1999). Chemically flavonoids are C$_6$-C$_3$-C$_6$ compounds, the two C$_6$ groups are substituted benzene rings and the C$_3$ group is an aliphatic chain which consists of a pyran ring (Robinson, 1991).

They comprises of biflavones, isoflavones, xanthones, chalcones, flavonones, flavonols and flavones (Cowan, 1999; Bylka *et al*., 2004). Flavonoids have been reported to play a key role against various human diseases like, inflammation, cancer, cardiovascular disease and against various allergies (Yao *et al*., 2004; Ferguson *et al*., 2004; Havsteen, 1983; Ma *et al*., 2004; Lyons-Wall and Samman, 1997; Moon *et al*., 2006).

They have also been effective against wide range of pathogens. Their mode of action may be due to their ability to complex with soluble proteins and with bacterial cell walls. They are also capable of disrupting the microbial membranes (Tsuchiya *et al*., 1996).

Many of the dietary flavonoids are also potential anti-cancerous agent and have effects against chemoprevention and chemotheraphy. The mode of action of flavonoids against cancer may be due to either of the reversal of multi-drug resistance, anti-oxidation, inhibition of angiogenesis, induction of apoptosis and differentiation, cell cycle arrest, anti-proliferation and carcinogen inactivation or a combination of all these mechanisms (Ren *et al*., 2003).

Flavonoids exhibit gastro-protective effect and several mechanisms have been proposed to testify them. They cause decrease of histamine secretion from mast cells by inhibition of histidine decarboxylase, an increase in the mucosal prostaglandin content and also reported to inhibit the *H. pylori* growth. Flavonoids are also free
radical scavengers which have been seen to play a key role in the erosive and ulcerative lesions of the gastrointestinal tract (Borrelli and Izzo, 2000).

The most studied anti-ulcer flavonoids are quercetin, naringin, anthocyanosides, silymarin and sophoradin derivatives (Di Carlo et al., 1999).

2.4.2.1 Naringin:

It is a flavonone glycoside. It is an important flavonoid found in the grapefruit and is known to give a bitter taste. It is metabolized to flavonone-naringenin complex in humans. It has been seen that the aglycones of naringin and hesperidin which are naringenin and hesperetin are found to occur naturally in the citrus fruits (Kumar et al., 2010).

Reports have shown the active role of naringin in preventing the gastric mucosa ulceration in many animal models like, ethanol-induced chronic ulcer, pyloric occlusion and restraint stress (Martin et al., 1993; Parmar, 1983; Motilva et al., 1992; 1993).

The gastro-protective action of naringin involves an increase in the viscosity and glycoprotein content of the gastric mucosa. Naringin is also known to possess superoxide anion scavenger and antioxidant properties (Martin et al., 1994; Robak and Gryglewski, 1988).

2.4.2.2 Quercetin:

Quercetin is found to be most abundantly available flavonoid molecule. It has shown to prevent the gastric mucosal lesions produced by pylorus ligation and cold restraint stress (Martin et al., 1988; 1993). Quercetin also causes an increase in the amount of neutral glycoproteins which are found to be the most abundant and essential in gastric mucosa (Di Carlo et al., 1999). Studies have also shown the anti-\textit{H. pylori} effect of flavonoids in a dose dependant manner in-vitro (Beil et al., 1995).

In this study, we have reported the potent antimicrobial activity of quercetin isolated and identified from the leaves of \textit{Datura metel} which have shown anti-\textit{H. pylori} activity.

2.4.2.3 Silymarin:
Silymarin is a flavono-lignan complex which can be isolated from the seeds of milk thistle, *Silybum marianum* (Katiyar *et al.*, 2008). Silymarin prevents the ulceration induced by histamine output in pylorus-ligated rats and the cold-resistant stress but is not known to prevent the formation of ethanol-induced gastric lesions. The anti-ulcer effect of silymarin could be due to its inhibitory mechanism on the lipoxygenase pathway and the avoidance of the leukotriene synthesis (Alarcon *et al.*, 1992).

**2.4.2.4 Anthocyanosides:**

Anthocyanosides or anthocyanins are specific chemical elements in plants that control pigmentation. They are known to be super-antioxidants. The bilberry or *Vacillium myrtillus* is a prime source of anthocyanosides and it prevents occurrence of ulcer. Anthocyanosides have shown protective effects in ulcer induced by pylorus ligation, reserpine, phenylbutazone and ulcer induced by acetic acid or stress (Magistretti *et al.*, 1988).

Anthocyanosides is responsible for the biosynthesis of the mucopolysaccharides and results in improving the efficiency of the mucus barrier of the gastric region (Magistretti *et al.*, 1988; Cristoni and Magistretti, 1987).

**2.4.3 Tannins:**

Tannins are a group of phenolic substances that possesses strong astringent property. They are found in bark, wood, leaves, and roots, fruits, wood, bark and leaves (Hoste *et al.*, 2006; Samuelsson, 1999). It is antimicrobial in nature due to its ability to inactivate the enzymes, microbial adhesins, transport proteins, cell envelope etc. Scalbert, (1991) have reported the antimicrobial and antifungal activities in tannins. The condensed tannins usually bind to the cell wall of the bacteria inhibiting its protease activity and growth.

Several plants containing tannins were reported to have anti-ulcer activity like, *Calliandra portoticensis* (leaves), *Linderae umbellatae* (stem), *Entandrophragma utile* (bark), *Mallotus japonicus* (bark), *Veronica officinalis* (aerial parts) and *Rhigocarya racemifera* (leaves). Ezaki *et al.*, (1985) have reported that anti-peptic and anti-ulcerogenic activity of *Linderae umbellatae* is mainly due to the presence of tannins.
Hydrolyzable tannins have been reported to have an in-vitro effect against *H. pylori* infection (Funatogawa *et al*., 2004). The compounds, tellimagrandin 1 and tellimangrandin 2 did not have any effect on the viability of MKN-28 cells derived from human gastric epithelium indicating that they might be good alternatives for treatment with minimal effects on the host.

### 2.4.4 Coumarins:

They are phenolic compounds made up of α-pyrone and fused benzene rings. Almost 1300 coumarins had been identified till the year 1996 (Cowan, 1999). Coumarins have shown anti-inflammatory (Piller, 1975), anti-thrombotic (Thastrup *et al*., 1985), antimicrobial (Cowan, 1999), vasodilatory activities (Namba *et al*., 1988). It was reported that hydroxyl coumarins like, 6,7-dihydroxy-4-methylcoumarin, 5,7-dihydroxy-cyclopentanocoumarin, 7-hydroxy-4-methylcoumarin and 6-hydroxy-7-methoxy-4-methylcoumarin showed comparable anti-*H. pylori* activity with metronidazole. Since, many *H. pylori* strains are reported to be resistant to metronidazole, the activity of hydroxyl coumarins may prove to be highly beneficial (Banatvala *et al*., 1994). Also, Basile *et al*., (2009) reported the anti-*H. pylori* activity of coumarins extracted from the roots of *Ferulago campestris* plant.

### 2.4.5 Essential oils and terpenoids:

Essential oils are aromatic volatile oils found in medicinal and other edible plants. These oils such as carvacrol and thymol are also food flavouring agents, they possess antimicrobial activity against a wide range of pathogens (Manohar *et al*., 2001).

Terpenoids are secondary metabolites which are rich in isoprene compounds and also associated with the fragrance of the plants. They occur as di, tri, tetra, hemi and sesquiterpenes. Almost 20,000 of these compounds have been isolated from the plant sources. Some of them are camphor, limonene, abscissic acid, aucubin, gossypol, gibberellic acid, menthol, eugenol, β-carotene and terpinen-4-ol (Njume *et al*., 2011).

Terpenenes or terpenoids have shown to be active against bacterial strains, viruses, fungi and protozoans. The terpenes are to be able disrupt the membrane by the lipophilic compounds (Cowan, 1999). Kadota *et al*., (1997) have reported anti-*H. pylori* activity of trichorabdal A, a diterpene. Terpenoids containing fractions from
Ptelopsis suberosa bark prevented the ulcer formation and improved the condition of the existing ulcers in rats which had been chemically induced (De Pasquale et al., 1995). More research is further required to understand the potential use of the terpenoids as anti-\textit{H. pylori} agents.

2.4.6 Alkaloids:

They are heterocyclic nitrogen compounds that are usually present in the ethanolic and methanolic plant extracts (Njume et al., 2009). Some of them are codeine, heroine, atropine, morphine, vincristine etc.

\textit{Datura metel} plant is a potential source of large number of alkaloids like hyoscine, hyoscyamine, meteloidine, scopolamine, tigloidine, tropine, withametelin and daturametelin (Rastogi and Mehrotra, 1998).

Hamasaki et al., (2000) have reported that the crude extract of fruits of \textit{Evodia rutaecarpa}, contains quinolone alkaloids namely, 1-methyl-2-[(Z)-7-tridecenyl]-4-(1H)-quinolone and 1-methyl-2-[(Z)-8-tridecenyl]-4-(1H)-quinolone. The antimicrobial activity of these compounds was highly selective towards the \textit{H. pylori} and was almost non-active against the other intestinal pathogenic strains. The results suggested that these alkyl methyl quinolone alkaloids could be useful in eradication of \textit{H. pylori} without affecting the other intestinal bacterial strains.

2.4.7 Mixtures:

The traditional medicine is based on the use of plant extracts both single and in combination to treat a wide range of human infections (Kumar and Singh, 1992). Extracts of \textit{Cleistanthus collinus} contain compounds like glycosides, arylnathalene lignin lactones (cleistanthin A and B, collinusin and oduvin) which have shown antimicrobial activities (Satyanarayana et al., 1984). Mitra et al., (1996) have reported the anti-ulcerogenic effect of a herbal formulation, UL409 which is a combination of six medicinal plants, \textit{Saussurea lappa}, \textit{Glycyrrhiza glabra}, \textit{Aegle marmelos}, \textit{Foeniculum vulgare}, \textit{Rosa damascene} and \textit{Santalum album}. The herbal formulation was gastroprotective in nature, prevented the ulceration induced by aspirin, ethanol, histamine, stress, indomethacin and pylorus ligation. Manonmani et al., (1994) reported the anti-ulcerogenic effect of a Cauvery-100 (C-100) formulation. C-100 consists of a mixture made up of many plants like, \textit{Cuminum...}
cyminum, Emblica officinalis, Trema orientalis, Vitis vinifera, Carum carvi, Withania somnifera, Eclipta alba, Embelia ribes, Citrnum limon, Picrorrhiza kurrooa, Glycyrrhiza glabra, Aegle marmelos and Zingiber officinale. This formulation was very much capable to decrease the volume and acidity of the gastric juice, decrease the number of lesions induced by indomethacin and increase the mucosal defense in the gastric region.

India has been a rich source of various herbal plants. Herbal plants have exhibited interesting results with numerous therapeutic activities for the treatment of various diseases. Since, plants and their secondary metabolites as alternative source of treatment have been highly effective, there has been an increasing demand in the use of herbal treatment globally. Herbal treatment has been into action since ancient times. These days many phytocompounds are readily available, cheaper and with less side effects which easens the general public to self medicate and use them indigenously against the treatment of various diseases (Sher, 2009).