3. OBJECTIVE AND PLAN OF WORK
3.1 Objective

Diarrhoea is a condition of passage of loose, watery stools with increased frequency. It is common in all age groups but children are more vulnerable. It is more common in poorly nourished children living in poor sanitary conditions (Mujumdar et al., 2006). Most cases of diarrhoea are due to infection in the alimentary canal by virus, bacteria, parasites and fungi. Milk and allergy to certain food substances can also give rise to diarrhoea. Certain medicines like antibiotics pain-killers and medicines for cancer can give rise to diarrhoea. Excessive, indigestible food substances and emotional factors can also give rise to diarrhoea (Farthing et al., 2000, Gilman, 1996).

The standard anti-diarrhoeal agents such as diphenoxylate, loperamide and deodorised tincture of opium have limited effects, and may cause central nervous system depression. Many patients with HIV and chronic diarrhoea have turned to herbal formulas for help, and studies have demonstrated the efficacy of such preparations for the treatment of diarrhoea (Seung et al., 2004, Cohen et al., 2004). Medicinal plants are promising source of antidiarrhoeal drugs. Arising from the trend toward reduced diarrhoea in patients receiving herbal preparation, many herbal formulas have been developed, even though they contain various mixtures of active constituents (Attia 2004).

Mebarid syrup, Enterocin syrup and Kutajarishta syrup are ayurvedic formulations, consist of medicinal herbs which are indicated in diarrhoea and dysentery. Different herbs used in these formulations have different effects to treat the diarrhoea and dysentery. Different medicinal activities shown by these herbs are:

- Checks intestinal hyperperistalsis, resolves intestinal colics and spasms, relieves abdominal pain (Kokate et al., 2007, Agarwal et al., 2005, Arul et al., 2004, Ashish et al., 1999).
- Reduces microbial assault by destroying them (Nadkarni, 1954, Gerald et al., 2007, Suchendra et al., 2007, Pillai, 1992).
- Checks electrolyte losses and toxicity (Gupta et al., 1992, Claudia et al., 2009, Kirtikar et al., 1988).
- Restores normal growth of intestinal flora (Swami Sadashiv, 2004, Chopra et al., 1982).
- Improves the resistance of the G.I. tract (Swami Sadashiv, 2004).
Though Mebarid, Enterocin and Kutajarishta are widely used in the treatment of diarrhoea and dysentery, still there is a paucity of data on the pharmacological evaluation, mechanisms of action and bio-standardisation of these formulations.

Black Pepper (*Piper nigrum*) is a wonderful spice with a rich history and many uses in the kitchen and in the medicine. In Sanskrit it is known as *Marich*, one of the name for the sun, as it is thought to be filled with solar energy. It is currently the world’s most widely traded spice appearing on the tables of cafes and restaurants everywhere (Kokate et al., 2007).

Black pepper is an aromatic pungent warming herb that lowers fever and improves digestion. Either powdered or its decoction is widely used in traditional Indian medicine. The ancient Aryans considered it as a powerful remedy for various disorders of the anatomical system and prescribed it as an effective cure for dyspepsia, malaria, delirium, tremors and hemorrhoids. It is used in ayurvedic medicine to stimulate the digestive system and used for the treatment of nausea, lack of appetite and other dyspeptic complaints. In Chinese medicine it is used to treat food poisoning, stomach chills, cholera, dysentery and vomiting caused by hypothermia. In west it is used for digestion and relieving gas (Pruthi, 1998, Agarwal et al., 2005).

Black pepper contain good amount of minerals like potassium, calcium, zinc, manganese, iron, and magnesium. Potassium is an important component of cell and body fluids that helps controlling heart rate and blood pressure. Manganese is used by the body as a co-factor for the antioxidant enzyme, superoxide dismutase. Iron is essential for cellular respiration and blood cell production. They are also excellent source of many vital B-complex groups of vitamins such as pyridoxine, riboflavin, thiamin and niacin. It is a rich source of many anti-oxidant vitamins such as vitamin-C and vitamin-A. They are also rich in flavonoids, polyphenolic anti-oxidants like carotenes, cryptoxanthin, zeaxanthin and lycopene. These compounds help the body to remove harmful free radicals and help to protect from cancers and diseases (Kokate et al., 2007, Agarwal et al., 2005).

The alkaloid piperine is the major constituent of black pepper. It is beneficial in many areas and conditions. It is said to increase thermogenesis - the process of generating energy in cells. Piperine has the ability to increase the bioavailability of certain nutrients
and drugs, such as: beta carotene, curcumin, selenium, pyroxi- dine (B6), glucose, and amino acids. It also increases the flavor of foods and alcohol (Jensen et al., 1998).

Some health benefits that can be gained from using piperine may be helpful in reducing inflammation, improving digestion, the reduction of pain, and the relief of asthma. It is also said that it improves the production of serotonin, a mood enhancer and pain relieving neurotransmitter. It is said that the nutrient could also relieve stomach ulcerations (Bai et al., 2000).

Piperine is known as central nervous system depressant and has good anticonvulsant and antimicrobial property. It stimulates both digestive and circulatory system. Piperine is used all over the world for various illnesses. In Mexico for instance, it is used to treat stomach aches, malaria, and as an anti-inflammatory agent. Morocco uses it to treat weight loss and leukemia. Indonesia uses it to reduce or prevent headache and fever, as a treatment for snake poisoning, and to treat epilepsy (Koul et al., 1993).

Despite the availability of several remedies to treat diarrhoea including botanicals and chemical agents, yet there is a great need for the evaluation of newer, economical and cost effective agents to meet the challenges of upcoming era regarding disease burden. Considering the significance of herbal formulations in diarrhoea over allopathic drugs which are having side effects, antidiarrhoeal activity and phytochemical analysis of herbal formulations like Mebarid, Enterocin, Kutajarishta and crude drug like black pepper was performed.

The objectives of the present work were:

i) To study the antidiarrhoeal activity of herbal formulations like Mebarid, Enterocin, Kutajarishta and Black pepper and its comparison with standard drug.

ii) To study the possible mechanisms of action of antidiarrhoeal activity of selected herbal formulations and Black pepper.

iii) To evaluate the possibility of application of pharmacological methods in the biostandardisation of the herbal antidiarrhoeal formulations.

iv) To study the effect of Black pepper extract on antidiarrhoeal activity of Mebarid, Enterocin and Kutajarishta.

v) To perform the phytochemical analysis of Mebarid, Enterocin, Kutajarishta and Black pepper.
vi) To isolate the Piperine from Black pepper and characterise it.
vii) To perform the antidiarrhoeal activity of Piperine.
3.2 Plan of work

To achieve the objectives of present study, the plan of work was:

1. Market survey of antidiarrhoeal herbal formulations with proven activity.
2. Literature survey for the reported antidiarrhoeal drugs of natural origin which has been used in antidiarrhoeal herbal formulations and Black pepper.
3. Procurement of Black pepper and marketed herbal formulations (Mebarid, Enterocin, Kutajarishta) having antidiarrhoeal activity.
4. Pharmacognostic study of Mebarid, Enterocin, Kutajarishta and Black pepper.
5. Standardization of Mebarid, Enterocin, Kutajarishta and Black pepper.
6. Pharmacological study (antidiarrhoeal activity) of Mebarid, Enterocin, Kutajarishta and Black pepper.
7. Phytochemical Analysis of Mebarid, Enterocin, Kutajarishta and Black pepper.
8. Extraction of Black pepper and isolation and characterization of Piperine.
9. Pharmacological study (antidiarrhoeal activity) of Piperine.