“From the bitterness of disease man learns the sweetness of health”

- Catalan

Endocrine disorder affects approximately one quarter of the population in developed countries. Thyroid dysfunction is one of the most commonly encountered endocrine abnormalities in India. Thyroid disease is being increasingly diagnosed with greater awareness and is one of the chronic non-communicable disease affecting women more, though male population is not spared of the ailment (James and Kumar, 2012).

Thyroid is a butterfly shaped organ situated in the neck region and is mainly concerned with the regulation of body’s metabolism (Nissanka, 2010). It is one of the largest endocrine glands in the body. The gland comprises of multiple follicles lined by follicular cells resting on a basement membrane. The follicles are filled by a clear viscous material called colloid. The colloid is a glycoprotein called thyroglobulin within which are incorporated the thyroid hormones. The thyroid gland controls the sensitiveness of the body to other hormones (Pal, 2007).

Thyroid secretes two metabolically important hormones namely triiodothyronine (T\textsubscript{3}) and thyroxine (T\textsubscript{4}). The thyroid gland also makes calcitonin, a hormone that helps to regulate calcium levels in the blood by inhibiting the breakdown (reabsorption) of bone and increasing calcium excretion from the kidneys. Iodine is an integral part of the thyroid hormones T\textsubscript{3} and T\textsubscript{4} which are necessary for normal growth and development (Skeaff, 2011).

About 90% of the secretory product released from the thyroid gland is in the form of T\textsubscript{4}. T\textsubscript{3} is the major biologically active form of thyroid hormone at the
cellular level. $T_3$ is about four times more potent than $T_4$ (Sherwood, 2011). Besides influencing every organ system and most biological processes in the body, the thyroid hormones have unique actions on growth and development during the first two decades of life. Most of the secreted $T_4$ is converted or activated to $T_3$ by the removal of one of its iodine. This primarily occurs in the liver and kidneys. About 80% of the circulating $T_3$ is derived from secreted $T_4$ that has been peripherally stripped. Thyroid hormone ($T_3$) has a profound influence on normal development, differentiation and metabolism (Wulf et al., 2008).

Thyroid gland plays a central role in the metabolism of iodine. The role of iodine in nutrition arises from the importance of thyroid hormones in the growth and development of humans and animals (Anon, 2006). Thyroid hormones are synthesized in the thyroid gland by iodination and coupling of two tyrosine molecules in a process which depends on the adequate supply of iodine (Banijamali, 2007). Iodine Deficiency Disorder (IDD) is the most common endocrinopathy in the world and also the most preventable cause of mental retardation. Children in endemic areas show retarded physical and mental development and low I.Q levels (Ahad and Ganie, 2010).

Thyroid gland regulates a wide array of metabolic processes. Thyroid hormone significantly affects lipoprotein metabolism as well as some cardiovascular disease (CVD) risk factors, thus influencing overall CDV risk. A slight increase in thyroid-stimulating hormone (TSH) results in a linear increase in total cholesterol (TC), low-density lipoprotein cholesterol (LDL-C) and triglycerides (TGs) and a linear decrease in high-density lipoprotein cholesterol (HDL-C) levels (Rizos et al., 2011).

Thyroid diseases have been recognized for more than a century. Abnormal thyroid function leads to thyroid disorders and are the most common among all the endocrine diseases in India. The two major functional thyroid disorders are hypothyroidism and hyperthyroidism. These disorders are eight
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Hypothyroidism is a common disorder affecting about 5% of people over the age of 60 years (Glasberg et al., 2006). Hypothyroidism ("Hypo" means "under" or "below") may be defined as the clinical condition in which the thyroid hormones falls below the body’s normal need. It results from reduced secretion of both T₃ and T₄ which leads to hyper secretion of thyroid stimulating hormone (TSH). Hypothyroid patients suffer from decrease in general health status, decrease in psychological function, working memory and motor learning (Samuels et al., 2008). Hypothyroidism may result in depression of myocardial function, decreased spontaneous ventilation, abnormal baro receptor function, reduced plasma volume, anaemia, hypoglycemia, hyponatraemia and impaired hepatic drug metabolism (Farling, 2010).

The term “hyperthyroidism” encompasses heterogenous group of disorders, all characterized by elevated levels of thyroid hormones in the blood. It is one of the uncommon thyroid disorders in childhood and adolescence. Hyperthyroidism may manifest as an enlarged thyroid (goiter), heart rate irregularities, tremor, sweating, palpitations, nervousness and increased activity and eye abnormalities (Souter, 2012).

Hyperthyroidism shows a hyperdynamic circulation with increased cardiac output, heart rate, pulse pressure and blood pressure and decreased vascular peripheral resistance, whereas the hypothyroid state is associated with low cardiac output, decreased heart rate, low pulse pressure and low blood pressure and elevated vascular peripheral resistance (Chopra et al., 2011).

Hypothyroidism is more prevalent than hyperthyroidism, mostly affecting women. Both the cases are found in elderly persons and many remain
undiagnosed and untreated thinking it as an old age problem. Drugs such as thionamides, lithium, perchlorate, aminoglutethimide, thalidomide, interferon-alfa, interleukin-2, iodine and iodine-containing drugs can cause hypothyroidism and drugs namely iodine, amiodarone and denileukin diftitox can cause hyperthyroidism (Economidou et al., 2011).

Hypothyroidism can be treated by hormone replacement therapy whereas hyperthyroidism can be treated with antithyroid drugs (ATDs), radioactive iodine therapy or surgery. Several antithyroid drugs are available but give an adverse effect in long term treatment. So, the usage of medicinal plant in the treatment of thyroid disorder could be exploited. Many herbs have been used in the treatment of thyroid dysfunction.

Herbs used in the treatment of hypothyroidism includes Ashwagandha root, Bladderwrack, Gum guggul, Milk thistle, Avena sativa (Green Oats), Myrrh, Coleus forskohlii (Makandi) and Sage (Schertell, 2010). Herbs commonly used for the treatment of hyperthyroidism are Lycopus europea (Bugleweed), Melissa officinalis (Lemon balm), Leonurus cardiac (Motherwort) and Prunella vulgaris (Self-heal) (Hughes, 2011) (http://www.herbalremediesworld.com).

In recent years, the plants used traditionally for curative purposes have attracted the attention of researchers. The use of traditional medicine is widespread and plants are still a large source of natural antioxidants that might serve as leads for the development of novel drugs (Khatun et al., 2011). Medicinal plants find application in pharmaceutical, cosmetic, agricultural and food industry. The use of medicinal herbs for curing disease has been documented in history of all civilizations. Medicinal herbs are significant source of synthetic and herbal drugs. Herbs and herbal products today symbolize safety in contrast to the synthetics that are regarded as unsafe to human and environment. The medicinal properties of plants have been investigated in the recent scientific developments throughout the world, due to their potent antioxidant activities, no side effects and economic viability (Sharma et al., 2012). India is the largest
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producer of medicinal plants and is appropriately called the botanical garden of
the world. Exploration of the unknown medicinal plants and known ones are
attempted in various region of India (Puratchikody and Swarnalatha, 2011).

Phytochemicals are non-nutritive plant chemicals that have protective or
disease preventive properties. Plant produces these chemicals to protect itself
but recent research demonstrates that many phytochemicals can protect
humans against diseases (Karthishwaran et al., 2010). Phytochemicals from
medicinal plants serve as lead compounds in drug discovery and design. WHO
estimated that more than 80% of world’s population still depends on traditional
remedies to meet their primary health care needs (Narmadha and Devaki,
2012). A large variety of phytochemicals commonly consumed with the human
diet influence health and may contribute to the prevention of disease.
Phytochemicals can be classified as carotenoids, phenolics, alkaloids, nitrogen-
containing compounds and organosulfur compounds. The most studied of the
phytochemicals are the phenolics and carotenoids. Plant sterols which exhibit
structural similarities to cholesterol reduce LDL-cholesterol levels in humans by
interfering with cholesterol intestinal absorption (Guine and Lima, 2012).

Free radicals and other reactive oxygen species are derived either from
normal metabolic process in the human body or from external sources such as
exposure to X-rays, ozone, cigarette smoking, air pollutants and industrial
chemicals (Kumar, 2011). Free radicals are implicated for more than 80
diseases including diabetes mellitus, atherosclerosis, cataract, rheumatism,
ageing and other auto immune diseases. In treatment of these diseases
antioxidant therapy has gained an utmost importance (Subhashini et al., 2011).

Numerous reports have highlighted the free radical scavenging
properties of phytochemical antioxidants such as polyphenols or carotenoids
(Carlsen et al., 2010). It appears today that the biological effects of such
antioxidants are more diverse and involve cell-mediated responses and the
modulation of various cell-signalling pathways (Shen et al., 2005; Scalbert et al.,
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2005; Stevenson and Hurst, 2007). Natural antioxidants are found in some vegetables, fruits and a variety of other foods (Moon & Shibamoto, 2009). Antioxidants have been used in food industry to prolong the shelf life of foods, especially those rich in polyunsaturated fats due to lipid peroxidation (Anokwuru et al., 2011). Nature has been a source of medicinal agent for thousands of years and an impressive number of modern drugs have been isolated from natural sources, many based on their use in traditional medicine (Fagbohun et al., 2012).

Seaweeds are one of the important constituents of the primary producers and contribute substantially to the carbon budget of the coastal ecosystem. Seaweeds have been used by human as medicine and food for at least 13,000 years (Thinakaran et al., 2012). Over the past several decades seaweeds and their extracts have generated an enormous amount of interest in the pharmaceutical industry as a fresh source of bioactive compounds with immense medicinal potential. They are rich in antioxidants such as carotenoids, pigments, polyphenols, enzymes and diverse functional polysaccharides (Vinayak et al., 2011). Seaweeds are excellent source of Vitamin A, B₁, B₁₂, C, D and E. Quality of protein and lipid in seaweeds are most acceptable for consumption compared to other vegetables mainly due to their high content in essential amino acids and relatively high level of unsaturated fatty acids (Lordan et al., 2011). The mineral nutrients present in seaweeds are diverse and the main elements being iodine and calcium. Oceans are the world’s main repositories of iodine and very little of earth iodine is actually found in the soil. The deposition of iodine in soil occurs due to volatilization from ocean water, a process aided by ultraviolet radiation (Patrick, 2008).

The brown algae are distinguished by their colour which varies from olive green through light golden to a rather deep shade of brown. This is because of the presence of a golden brown xanthophyll pigment fucoxanthin (C₄H₅O₆) in their chromatophores. Sargassum species are found to have the highest free
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radical scavenging property (Wijesekara et al., 2012). Sargassum was used to prevent goiter in ancient China and is regarded as one of the best marine biological resources for preventing IDD. Sargassum contains various secondary metabolites such as phlorotannins with biological activities (Cadena, 2010). It has also been used as an expectorant for chronic bronchitis, hypertension, and more frequently for edema, goiter and tuberculosis of lymph nodes (Hwang et al., 2010).

Maize is one of the most important food crops in semiarid tropics and it constitutes the main source of food energy for many poor people. Maize hair or corn silk is a collection of the stigmas from the female flowers of the maize plant. Corn silks are scientifically referred as Maydis stigma or Zea mays hair as they reflect the soft, fibre-like growth which accompanies the ear of the corn (Rosli et al., 2010). Corn silk is a traditional herbal medicine in India, which has been used in many parts of the world for the treatment of edema as well as for cystitis, gout, kidney stones, nephritis, prostatitis and similar ailments. Chronic consumption of maize gradually developed a relative state of biochemical as well as morphological hypothyroidism even in presence of adequate iodine in circulation (Chandra et al., 2009). Therefore, Zea mays L. could be used in treatment of hyperthyroidism.

Therefore Sargassum wightii Greville and Maydis stigma were selected for the present study as they have been used in the treatment of various ailments.

Hence the present study entitled “Influence of drug therapy in thyroid disorder patients and the effect of Sargassum wightii Greville and Maydis stigma on experimentally induced hypo and hyperthyroidism in Swiss albino rats” was carried out with the following objectives:

- To assess the clinical and biochemical status of hypo and hyperthyroid patients before and during the treatment.
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- To analyze the phytochemical components and iodine content of *Sargassum wightii* Greville (Brown algae - seaweed) and *Maydis stigma* (*Zea mays* hair - sweet corn silk).

- To evaluate the free radical scavenging activity of *Sargassum wightii* Greville and *Maydis stigma*.

- To determine the total antioxidant activity of *Sargassum wightii* Greville and *Maydis stigma*.

- To find out the bioactive components in *Sargassum wightii* Greville and *Maydis stigma* samples.

- To assess the effect of methanolic extracts of *Sargassum wightii* Greville and *Maydis stigma* on experimentally induced hypo and hyperthyroidism in Swiss albino rats.