4. DISCUSSION

Seaweeds or marine macrophytic algae are an assemblage of the members of Chlorophyceae, Phaeophyceae and Rhodophyceae and are the common inhabitants of the tidal and intertidal environments of the marine ecosystem. Seaweeds have some of the valuable medicinal components such as antibiotics, laxatives, anticoagulants, anti-ulcer products and suspending agents in radiological preparations. The edible seaweeds contain a significant amount of the proteins, vitamins and minerals for human nutrition (Mohamed et al., 2005). Marine algae can serve as a source of minerals, vitamins, free amino acids and polyunsaturated fatty acids. The use of algal oils containing Long Chain Polyunsaturated Fatty Acids (LCPUFAs) as nutritional supplements has been recommended (Calder and Grimble, 2002) and algal sources are being identified for the presence of Docosahexaenoic Acid (DHA) and Eicosapentanoic Acid (EPA).

Compounds with cytostatic, antiviral, antihelminthic, antifungal and antibacterial activities have been detected in brown algae (Lindequist and Schweder, 2001 and Newman et al., 2003). With marine species comprising approximately a half of the total global biodiversity, the sea offers an enormous resource for novel compounds and it has been classified as the largest remaining reservoir of natural molecules to be evaluated for drug activity.

Recently, a number of studies have been reported on the phytochemistry of seaweeds across the world (AL-Haj et al., 2010,
Salem et al., 2011 and Manivannan et al., 2011). Chakraborty and Paulraj (2010) and Liu et al. (2012) reported that seaweeds are rich source of bioactive compounds such as terpenoids, phlorotannins, fucoidans, sterols and glycolipids and the extracts or isolated pure components from seaweeds possess a wide range of pharmacological properties such as anticancer, antibacterial, antifungal, anti-viral, anti-inflammatory, anticoagulant, antioxidant, hypoglycaemic, hypolipidemic, antimelanogenic, antiboneloss, hepatoprotective and neuroprotective activities.

Marine algae synthesize active compounds which are used in conventional and complementary medicine. Different varieties of marine algae were reported to have active ingredients that can cure diseases. Currently large proportions of population prefer to use remedies of natural origin for curing illness as these claimed to produce less side effects. Marine organisms are emerging as good candidates as an alternate source for bioactive substances in pharmaceutical industry and also as a source of food and other health aspects.

Earlier reports indicated that the extracts of brown seaweeds belonging to *Turbinaria* sp. were found to have antioxidant and anti-inflammatory activities (Zubia et al., 2009 and Vijayabaskar and Shiyamala, 2012). Additionally, these species have essential nutritional components like mineral salts (K, Ca, and Fe), soluble fibers, digestible protein and polyunsaturated fatty acids. More than these, seaweeds are also a wealthy resource of dietary iodine and fibers which can also play an immense part in enhancing the food quality and maintenance of health (Gupta and Ghannam, 2011).
According to Stansbury et al. (2012) seaweeds are the major source of minerals especially iodine in addition to other nutrients, thus seaweed is chosen as a natural remedy to explore its effectiveness for the management of methimazole induced hypothyroidism in albino rats.

On the basis of traditional and pharmaceutical uses, brown algae namely Turbinaria conoides and Sargassum wightii, red algae namely Gracilaria verrucosa, Gracilaria corticata and Kappaphycus alvarezii have been selected from Tamil Nadu, Rameswaram, India for the present study.

Alkaloids are commonly found to have antimicrobial, cytotoxic and antiplasmodic properties as reported by Omulokoli et al. (1997) and Srivastava et al. (2010). According to Chakkaravarthy and Kumar (2009) terpenoids have antioxidant activity. In the present study proteins, alkaloids and terpenoids were present in significant amounts in brown algae, T. conoides and red algae, G.verrucosa. Similar results were reported by Dinesh et al. (2007) and Nirmal et al. (2014) which confirms the present study.

Saponins are considered as a key ingredient in traditional Chinese medicine and are responsible for most of the observed biological effects. Tannins are used therapeutically as antiviral, antibacterial, antiulcer and antioxidant agents. Many tannin containing drugs are used in the treatment of piles, inflammation, burns and as astringent (Kolodziej and Kiderlen, 2005). Steroids of plant origin are known to be important for insecticidal, antimicrobial, antiparasitic and cardiotonic properties. In the present study,
saponins were noticed in most of the seaweed extracts whereas tannins were present moderately in ethanolic extract of *T. conoides* and *G. verrucosa*, steroids, quinones were present only in brown algae and cardioglycosides were present in *T. conoides*, *G. verrucosa*, *S. wightii* and *K. alvarezii*. The results of the present study are in agreement with the studies reported by Guru *et al.* (2013) and Senthil *et al.* (2013).

The various phytochemicals detected from the seaweeds are known to have beneficial importance in industrial and medical sciences (Jeeva *et al.*, 2012 and Sudharsan *et al.*, 2012). Thus the present study suggests that the seaweed extracts possessed phytochemical compounds thereby supporting their folkloric usage against various ailments.

Flavonoids have been reported as antioxidants, scavengers of a wide range of reactive oxygen species and inhibitors of lipid peroxidation and also as potential therapeutic agents against a wide variety of diseases (Sava and Sirbu, 2010 and Amudha and Pari, 2011). In the present study, the ethanolic extract of brown seaweed, *T. conoides* has flavonoid content of $2.89 \pm 0.05$ mg QE/g followed by ethanolic extract of *Sargassum wightii* exhibiting $2.12 \pm 0.07$ mg QE/g which is in accordance with results achieved by Ejaz *et al.* (2014) and Anjana *et al.* (2014).

Phenolic compounds can act as antioxidants by chelating metal ions, preventing radical formation and improving the antioxidant status of endogenous system. The polyphenols are generally more soluble in polar organic solvents like ethanol, methanol or acetone. In the present study, the
total phenolic content of ethanolic extracts were found to be more than the other extracts, with *G. verrucosa* having the highest total phenolic content of 201.80 ± 1.0 mg GAE/100 gm followed by *T. conoides* having 184.23 ± 0.16 mg GAE/100 gm. The present findings coincide with the reports by Amir *et al. (2013)* and Janarthanan and Kumar (2013).

Shahidi (2008) reported antioxidant activity of marine algae may arise from pigments such as chlorophylls and carotenoids, vitamin and vitamin precursors including α-tocopherol, β-carotene, niacin, thiamine and ascorbic acid, phenolic such as polyphenolic and hydroquinones and flavonoids, phospholipids particularly phosphatidylcholine, terpenoids, peptides and other antioxidative substances, which directly or indirectly contribute to the inhibition or suppression of oxidation processes. The Phaeophyta (brown seaweeds) shows comparatively higher antioxidant activity than green and red algae (Al-Amoudi *et al.*, 2009). In the present study the total antioxidant content was highest in ethanolic extract of brown algae, *T. conoides* having 210.4 ± 1.5 mg AAE/g followed by red algae *G. verrucosa* showing 202.7 ± 0.62 mg AAE/g when compared to other seaweed extracts. Similarly findings were reported by Meenakshi *et al.* (2009) and Indu and Seenivasan (2013).

Free radicals are responsible for causing various human diseases. An antioxidant can scavenge free radicals, thus plays an important role in the prevention of free radical-induced diseases. By donating hydrogen radicals, the primary radicals are reduced to non-radical chemical compounds (Jadhav *et al.*, 1995 and Yamaguchi *et al.*, 1998). One major action of antioxidants in
cells is to prevent damage caused by the action of reactive oxygen species. The effect of antioxidants on DPPH radical scavenging is thought to be due to hydrogen donating ability. Hence DPPH has been used extensively as a free radical to evaluate the free radical scavenging activities of compounds (Duan et al., 2006). The present findings showed that ethanolic extract of *T. conoides* gave the highest DPPH scavenging activity among the various extracts. The IC$_{50}$ of ethanolic extract of *T. conoides* was found to be 5 mg/ml. The smaller IC$_{50}$ value corresponds to the higher antioxidant activity of the seaweed extract. This indicated that among the seaweeds selected, *T. conoides* was rich in antioxidants. This was in accordance with the results of Gopalraj et al. (2011), Sarojini et al. (2013) and Indu and Seenivasan (2013).

Reducing capacity is considered as a significant indicator of potential antioxidant activity of a compound or sample. The reducing power property indicates that the antioxidant compounds are electron donors and can reduce the oxidized intermediates of the lipid peroxidation process, so that they can act as primary and secondary antioxidants (Yan and Chen, 1995). In the present study, brown algae ethanolic extract of *T. conoides* possessed the highest ferric reducing ability of 800.8 ± 0.50 μmoles Fe(II) / g dry weight when compared to other seaweed extracts which falls in line with the findings of Meenakshi et al. (2012), Megha and Anjali (2013) and Jayalakshmi et al. (2014).

Malondialdehyde (MDA) is the major degradation product of lipid hydroperoxides used as a marker for assessing the extent of lipid peroxidation
in clinical diagnosis (Fukunaka et al., 1995). The lower values in millimoles of MDA equivalent compounds formed/kg (MDAEC/kg) indicate a higher lipid peroxidation inhibitory effect. In the present study, the ethanolic extract of *T. conoides* produced minimum amount of MDA (8.6 nmoles ± 0.11 MDA/g) when compared to other seaweed extracts which was in agreement with the results obtained by Boonchum et al. (2011) and Rajauria et al. (2012).

According to Ensminger et al. (1995), seafood including seaweeds is known to be one of the richest sources of minerals. They are iodine, magnesium, calcium, phosphorus, iron, potassium, copper and fluoride. Seaweed, being high in numerous minerals and halides including iodine enhances thyroid function when consumed in appropriate amounts. Goitre is only one sign of iodine deficiency. Iodine deficiency can also cause oxidative stress in the body (Chanoine, 2003). When iodine is not present to produce thyroid hormones, high levels of TSH results and it leads to the formation of free radicals. Teas et al. (2004) reported that iodine which is usually present in seafood, is particularly abundant in brown algae whereas green seaweeds shows low iodine content. According to Matelijan (2006) addition of iodine to the aminoacid tyrosine in the thyroid glands helps in the production of thyroid hormones.

In the present study, the iodine content was highest in *T. conoides* with 27 mg/g algae followed by 16 mg/g in *S. wightii* which was in agreement with the findings of Solimabi et al. (1981) and Hou et al. (1997). The tyrosine content was maximum in ethanol extract of *T. conoides* having 3 ± 0.05 mg/g algal extract when compared to other extracts which was in
accordance with the results observed by Lewis and Gonzalves (1960) and Lewis (1962b).

From the in vitro studies conducted, the ethanolic extract of brown algae, *Turbinaria conoides* was found to contain more amount of bioactive compounds and possess significant antioxidant activity than the other extracts and thus was selected for animal studies.

Hypothyroidism is associated with increase in body weight due to a decrease in metabolism (Perveen et al., 2012). In the present study, Methimazole induced hypothyroidism in (group V) rats showed a significant increase in body weight than the control rats. This increase in body weight may be due to a decrease in the production of thyroid hormones or may be due to disturbances in food and water intake by the animals. Similar results were reported by Idris (2014). A gradual decrease in body weight was observed in group VII, VIII and IX (methimazole induced hypothyroidism) rats when treated with different concentrations of ethanolic extract of *T. conoides* and with the standard drug thyroxine. Dietary fibers present in the seaweed may aid in weight loss by prolonging the gastric emptying rate, thereby enhancing satiety and resulting in a reduction in food intake. This was in agreement with the results obtained from Jin-Song et al. (2006). Similar results were also reported by Bhaigyabati (2012) where the methanolic extract of *Sargassum wightii* showed a potent effect on thyroid status in hypothyroid rats which was indicated by a decrease in the body weight of the experimental rats which may be due to various phytochemicals present in it.
The weight of thyroid gland in hypothyroidism (group V) induced rats was increased when compared to control rats. The gain in weight might be due to increase in the body weight and due to development of goitre. It was in accordance with the results obtained by Chandra et al. (2004). Group III (protective effect) did not show much increase in weight of thyroid gland when compared to group V (untreated) hypothyroid rats thus showing the protective effect of *T. conoides* on hypothyroidism. Group VII, VIII and IX (methimazole induced hypothyroidism) rats treated with different concentrations of ethanolic extracts of *T. conoides* and standard drug thyroxine showed a decrease in the weight of thyroid gland. The weight of thyroid gland was brought down by treatment with ethanolic extract of *T. conoides* as it promotes the production of thyroid hormones. Similar results were observed by Chandra et al. (2009) and Hayat et al. (2010).

The amount of the thyroid hormones T₃ (triiodothyronine) and T₄ (thyroxine) in the blood plasma are considered a substantive evaluation of thyroid function (Mariotti, 2011). The best way to detect thyroid dysfunction is to measure the TSH level in blood sample. A high TSH level indicates an underactive thyroid gland (primary hypothyroidism).

The results of the present study showed a decrease in the levels of T₃ and T₄ and an increase in the levels of TSH in methimazole induced hypothyroidism group V rats. It is in agreement with the findings of Mansoor et al. (2011). An increase in levels of thyroid hormones of group VII, VIII and IX (methimazole induced hypothyroidism) rats were observed after treatment with the different concentration of ethanolic extract of *T. conoides*
and standard drug thyroxine. The increase might be due to presence of significant amount of iodine and tyrosine in the brown algae required for the production of thyroid hormones. The TSH level correlated well inversely with T₃ and T₄ levels. Control rats treated with T. conoides (group II) showed a gradual increase in T₃ and T₄ levels and decline in TSH levels. Thus the present findings clearly indicated that selected seaweed extract was a stimulant to thyroid functions. Group III rats showed no significant changes in T₃ and T₄ levels but levels of TSH was not increased as much as Group V (untreated) hypothyroid rats. This showed the protective function of the brown seaweed, T. conoides. The present findings are in accordance with Elghait et al. (2011). Similar studies were represented by Bhaigyabati (2012) who reported decreased levels of T₃ and T₄ and increased levels of TSH in methimazole induced hypothyroidism in rats and the levels were restored back to normal with the treatment of different concentrations of a brown algae Sargassum wightii Greville. The efficacy of Sargassum wightii Greville to cure experimentally induced hypothyroidism may be due to the presence of steroid and sterols in the extract (Seki et al., 2003). The present findings are also in agreement with Khalawi et al. (2013) and Khachatryan (2014).

The biosynthesis of thyroid hormone from thyroglobulin is catalyzed by thyroid peroxidase (TPO), an integral membrane protein. As the activity of TPO was depleted, the level of thyroid hormones declined. In the present study methimazole induced hypothyroid (group V) rats showed a significant decline in TPO levels. It is in agreement with Hasan et al. (2011) and Singla and Shashi (2013). Group III (protective effect) rats showed a lesser decline
in the TPO levels when compared to Group V (untreated) hypothyroidism induced rats. This shows the protective function of ethanolic extract of *T. conoides*. Group VII, VIII and IX (methimazole induced hypothyroidism) rats treated with ethanolic extract of *T. conoides* and the standard drug thyroxine showed an improvement in levels of TPO. Similar reports were observed by Chandra *et al.* (2004) and Chandra *et al.* (2009).

Thyroid hormones have significant effects on the synthesis, mobilization and metabolism of lipids. Overt hypothyroidism is associated with significant increase in circulating concentration of total cholesterol, triglycerides and low density lipoprotein (LDL) (O’Brien *et al.*, 1993). The presence of hypercholesterolemia in clinical hypothyroidism is well established by Erem (2006).

In the present study Group II rats treated with ethanolic extract of *T. conoides* showed a decrease in levels of total cholesterol, triglycerides and LDL-C and no significant increase in HDL-C. Methimazole induced hypothyroidism in Group V rats showed a significant elevation in serum levels of lipid profile (cholesterol, triglyceride and LDL) and a decrease in HDL-C which was in agreement with the findings of Pearce *et al.* (2008) and Saleh (2015). Group III rats (protective effect) showed a much lesser levels of total cholesterol, triglycerides and LDL-C when compared to Group V (untreated) hypothyroidism induced rats, thus confirming the protective effect of *T. conoides*. Group VII, VIII and IX (methimazole induced hypothyroidism) groups treated with different concentrations of *T. conoides* and standard drug thyroxine resulted in decreased levels of total cholesterol,
triglycerides, LDL-C and increase in HDL-C. The results obtained in this study is supported by the findings of Krishnamurthy et al. (2012). Bhaigyabati (2012) reported that methanolic extract of brown algae, *Sargassum wightii* Greville showed decreased levels of total cholesterol, triglycerides and LDL-C and increased levels of HDL-C in methimazole induced hypothyroidism in albino rats which is in accordance with the present study. It is suggested that the decrease in levels of total cholesterol, triglycerides may be due to phytosterols present in seaweeds.

The results in the present study shows that ethanolic extract of *T. conoides* is useful in the management of both hypothyroidism as it increases the T₃ and T₄ hormone levels and decreases TSH as well as in hypercholesterolemia where it decreases the total cholesterol levels. The results of this study indicate an association between hypothyroidism and lipid alterations. Reductions in LDL-C levels are important for delaying or inhibiting atherosclerosis, allowing plaque stabilization with a lower risk of erosion.

Hypothyroidism is one of the most common endocrinopathies worldwide and its incidence is increasing rapidly as reported by Unnikrishnan and Menon (2011). It is frequently found to coexist with both type 1 and type 2 diabetes mellitus (Kalra *et al.*, 2012 and Demitrost and Ranabir, 2012).

Interest in the hypoglycemic effect of hypothyroidism began a century ago, even before insulin was discovered (Janney and Isaacson, 1918). The hypoglycemia in hypothyroidism, dyspituitarism and Addison’s disease is
known to be common (Simpson, 1927). Moreover, literature clearly highlights the importance of hypothyroidism as a precipitating factor for hypoglycemia (Shah et al., 1975).

On the other hand, modern reviewers have clearly emphasized that hypothyroidism is one of the endocrine deficiencies responsible for hypoglycaemia (Samaan, 1989). Kalra et al. (2015) reported that hypothyroidism is linked with various hormonal, biochemical and nervous system abnormalities which may contribute to hypoglycemia.

Thyroid hormones also influence protein synthesis and cell growth. Hypothyroidism is generally associated with the reduction of the protein synthesis followed by decreased content of tissue protein. Due to depletion in the levels of glucose, proteins may be utilized as a source of energy, thereby mobilisation of proteins causes a reduction in total proteins. In the present study, the methimazole induced hypothyroidism in group V rats showed a significant decline in the blood glucose levels and a mild decline in serum total proteins which is similar to the findings of Kalra et al. (2015). Group VII, VIII and IX (methimazole induced hypothyroidism) rats treated with ethanolic extract of T. conoides and thyroxine showed an improvement in the levels of blood glucose and total proteins which is in agreement to Brown et al. (2014).

According to Khalid et al. (2006), in hypothyroidism serum creatinine increased and GFR decreased compared to the control group. The changes in serum creatinine levels develop rapidly and appear to be reversible. Earlier
findings by Kreisman and Hennessey (1990), Allon et al. (1990), Montenegro et al. (1996), Verhelst et al. (1997) and Jan (2005) reported an increased serum creatinine and decreased glomerular filtration rate and renal blood flow in primary hypothyroidism.

According to Basu and Mohapatra (2015), thyroid dysfunction affects renal physiology and development and vice versa. Disorders of the thyroid and kidney may co-exist with common etiological factors.

In the present study, the methimazole induced hypothyroidism in rats (Group V) showed elevated levels of serum creatinine and urea when compared to the control (Group I) rats. Similar reports were obtained by Arora et al. (2009), Saini et al. (2012) and Kumar (2013), indicating possible renal and hepatic damage. These two are considered as the major indices of impaired kidney and hepatic functions (Lindeman, 1990) and their increased level in the serum of hypothyroid rats may be due to reduction in glomerular filtration rate (GFR) (Montenegro et al., 1996). Group VII, VIII and IX (methimazole induced hypothyroidism) rats treated with ethanolic extract of T. conoides and thyroxine showed a decline in the levels of urea and serum creatinine which is in agreement with the findings of Camacho et al. (2003), Lippi et al. (2008) and Abdemula et al. (2013).

Increase in uric acid level in hypothyroidism induced rats may be either due to increased production because of myopathy associated with hypothyroidism or due to decreased renal clearance of uric acid as reported by Yokogoshi and Saito (1996). Hypothyroidism is associated with
hyperuricemia and impaired renal function (Giordano et al., 2001). Moreover, hyperuricemia in hypothyroidism is associated with increased serum creatinine and decreased creatinine clearance. In the present study, methimazole induced hypothyroidism in group V rats showed an increase in the levels of uric acid which was similar to results obtained by Chaudhury et al. (2013).

Group VII, VIII and IX (methimazole induced hypothyroidism) rats treated with ethanolic extract of *T. conoides* and thyroxine showed a decline in the levels of uric acid thus proving the protective effects of brown seaweed, *T. conoides* which is accordance with the findings of Kumar (2013).

Hypothyroidism may have features that mimic liver disease (pseudo-liver disease) like myalgias, fatigue and muscle cramps in the presence of an elevated aspartate aminotransferase from myopathy (Laycock and Pascuzzi, 1991). There is also evidence that hypothyroidism may directly affect the liver structure or function. Low ALP may also be associated with hypothyroidism.

Serum AST, ALT and CPK levels are significantly elevated in hypothyroidism. This is most likely due to muscle dysfunction rather than cardiac or other disorders. Musculo-skeletal disorders often accompany thyroid dysfunction (Cakir et al., 2005 and Malik and Hodgson, 2002).

Activities of various enzymes, especially those of Creatine Phosphokinase (CPK, EC 2.7.3.2) and Lactate Dehydrogenase (LDH, EC 1.1.1.27) are measured in plasma to assist in the diagnosis of myocardial
infarction. Primary hypothyroidism is associated with an increased incidence of arteriosclerosis.

In the present study, methimazole induced hypothyroidism group V rats showed activity of Alkaline phosphatase that was found to be closer to the control Group I rats whereas activities of Aspartate Transaminase and Alanine Transaminase were increased. Similar findings were reported by Thomsom et al. (1978) and Mane and Bhagwat (2011). Lactate dehydrogenase (LDH) and creatine phosphokinase (CPK) were elevated in untreated hypothyroid Group V rats. Elevated levels of CPK were reported by Finstrer et al. (1999), Ranka and Mathur (2003), Cinamon (2004) and Prakash et al. (2007) in hypothyroid patients. The levels of LDH was increased in untreated hypothyroid rats which was similar to the findings reported by White and Walmsley (1984). These enzymes in plasma that have increased activity are cytosolic in origin, leading to the suggestion that in primary hypothyroidism there is increased cell permeability and leakage as reported by Griffith and Hodgson (1965) and Doran and Wilkinson (1975).

Treatment of Group VII, VIII and IX (methimazole induced hypothyroidism) rats with ethanolic extract of *T. conoides* and standard drug thyroxine showed an improvement in the activity of Alkaline Phosphatase and decline in the activity of Aspartate Transaminase, Alanine Transaminase, Lactate Dehydrogenase and Creatine Phosphokinase. Similar reports were obtained by Goldman et al. (1977) and Kumar and Kar (2013).
The first line of defence against O$_2$ and H$_2$O$_2$ mediated injury are antioxidant enzymes such as Superoxide Dismutase (SOD), Glutathione Peroxidase (GPx) and Catalase (CAT). The second line of defence includes the antioxidants like Reduced Glutathione (GSH), vitamin C, vitamin E (mainly $\alpha$-tocopherol), albumin, carotenoids and flavonoids (Kale et al., 2007).

Yilmaz et al. (2003) and Europa et al. (2008) reported that hypothyroidism induces selective oxidative stress, increased levels of malondialdehyde, associated with decreased levels of CAT in the liver, amygdala and hippocampus of rat. Treatment with T$_4$ significantly restored their levels to normal. This clearly indicates that the changes in the levels of lipid peroxidation and antioxidant enzyme activities, which were determined in different tissues of hypothyroid rats are due to hypothyroidism. Moreover, excess thyroid stimulating hormone (TSH) is known to directly produce oxidative stress which was in agreement with the present results. Simultaneous oxidative damage to lipids and proteins lead to increased MDA. Hypothyroidism induced dysfunction of the respiratory chain in the mitochondria leads to accelerated production of free radicals such as lipid peroxides which consequently leads to oxidative stress (OS).

In the present study, methimazole induced hypothyroidism in Group V rats showed a decrease in the activities of Superoxide Dismutase (SOD), Glutathione Peroxidase (GPx) and Catalase (CAT) and Reduced Glutathione (GSH) levels and increase in the levels of malondialdehyde when compared
to the Group I control rats which was in accordance to the results of Pasupathi and Latha (2008), Elghait et al. (2011) and Kar and Sinha (2014).

The seaweeds not only exhibited excellent free radical scavenging activity but also were potent in suppressing TBARS formation by H₂O₂ induced lipid peroxidation in RBC. Hence the ability of the seaweeds to prevent lipid peroxidation was assessed in RBC by inducing lipid peroxidation with H₂O₂. In the present study Group VII, VIII and IX (methimazole induced hypothyroidism) rats treated with ethanolic extract of *T. conoides* and thyroxine showed an increase in activity of Superoxide Dismutase (SOD), Glutathione Peroxidase (GPx), Catalase (CAT) and Reduced Glutathione levels (GSH) and decrease in the levels of malondialdehyde which was found to have values better than the control group. Similar findings were reported by Kumar and Kar (2014) and Bahr and Ibrahim (2015). Thus methimazole induced hypothyroidism rats caused changes in antioxidant defence systems and peroxidation in tissues which can be reversed by the selected seaweed, *T. conoides* which is a natural iodine supplement.

To support the biochemical changes, the histological studies were also carried out in the present study.

Histology of Group V untreated hypothyroid rats showed follicles with luminal obliteration and showed the presence of microfollicles and scanty colloid when compared to Group I control rats. Some of the follicles were completely devoid of colloid and also lacked absorptive vesicles when induced with methimazole. These features suggested that there is a marked
suppressed functional status of the thyroid gland which is in agreement with Zaidi et al. (2004).

Group VII, VIII and IX (methimazole induced hypothyroidism) rats treated with ethanolic extract of low and high dose of *T. conoides* and standard drug thyroxine showed improvement in the morphology of thyroid gland tissues.

Chandra et al. (2009) reported that in control rats, thyroid follicles were lined by low cuboidal epithelial cells filled with colloid and all the follicles were almost equal and regular in size which was in accordance to the present study. In the present study there was an increase in the number of irregularly shaped small follicles filled with relatively less colloid, showing hypertrophic and hyperplastic follicular epithelial cells in the thyroid tissues. Variation in the number and size of follicular cells and colloid content were also observed. This is in agreement with the findings reported by Bhaigyabati (2012) showing the management of hypothyroidism by *Sargassum* extract. In addition, the colloid stained more intensely with eosin. Thyroid follicles in treated rats were lined with high follicular epithelial cells containing less colloid, reduced in size, irregular in shape and stained deeply with eosin. Deeply stained eosinophilic colloid in the follicles of the treated animals indicated that the entry of iodine into the follicles for synthesis of thyroid hormones which is similar to changes observed by Gaitan et al. (1989).

Thus this study indicates the significant role of seaweed for the management of hypothyroidism which may be due to the considerable amount of polyphenols, antioxidants, minerals, vitamins etc.