Organic chemists have always been looking at nature with curiosity and was wondering how it brings about all the changes in nature and in living systems. Soon they discovered that the molecules present in living organisms can not only be created by the creator but also by man in the test tube by the synthesis of urea by Wohler. The wonder of creation in nature lies in the making and breaking of bonds to produce newer and newer, bigger and bigger molecules. The organic chemist has started mimicking nature by synthesizing the molecules with fascinating and complex structures. Since then millions of organic molecules have been synthesized by chemists to cater to the needs of mankind as drugs, dyes, cosmetics, probes, pesticides, herbicides, fungicides, etc., and a variety of compounds for the use in day-to-day life.

A non-classical heating technique using microwaves, termed “Bunsen burner of the 21st century”, is rapidly becoming popular and is dramatically reducing reaction times. The significant outcome of microwaves (MW) assisted green chemistry endeavors, which have resulted in the development of synthetic protocols for drugs and fine chemicals synthesis that are relatively more sustainable. The use of emerging MW-assisted chemistry techniques in conjunction with green reaction media is dramatically reducing chemical waste and reaction times in several organic syntheses and chemical transformations (Kappe, 2004; Dallinger and Kappe, 2007). The synthetic chemistry community has been under increased pressure to produce, in an environmentally benign fashion, the myriad of heterocyclic systems required by society by routes that are shorter in time, and one of the best options to accelerate these synthetic processes is to use MW technology. Heterocyclic compounds hold a special place among pharmaceutically significant natural products and synthetic compounds (Polshettiwar and Varma, 2007). The remarkable ability of heterocyclic nuclei to serve both as biomimetics and as reactive pharmacophores have largely contributed to their unique value as traditional key elements of numerous drugs (Varma, 1999; Eicher and
Hauptmann, 2003). The efficiency of MW flash-heating has resulted in dramatic reduction in reaction times (a reduction from days and hours to minutes and seconds). The time saved by using a MW heating approach is potentially important in traditional medicinal chemistry and assembly of heterocyclic systems (Polshettiwar and Varma, 2007; Varma, 2006; Strauss and Varma, 2006).

Coumarins, benzothiazoles and thiazoles are three important heterocyclics which have been of much interest to chemists and pharmacologists from 17th century itself and have extensive uses. These uses include analgesic, anaesthetic, anti-allergic, anti-inflammatory, immunoregulatory, cholesterol lowering, anthelminitic, anti-tissuessive, anti-tumour, anti-tubercular, anti-arthritic, immunosuppressive, psychoactive, florescent dyes, solvatochromic dyes and several other activities (Richard et al., 1997, Kulkarni et al., 2006).

1.1 Coumarin

Coumarin (1) (known as 1,2-benzopyrones or o-hydroxycinnamic acid-8-lactones) is a chemical compound found in many plants, notably in high concentrations in the tonka bean, woodruff, and bison grass. Coumarin has a powerful anaesthetic action and has been recommended for use in laboratory experiments on animals. It readily excites vomiting in man, which renders it unsuitable as a hypnotic. Coumarin is used in perfumery, not only on account of its own fragrance, but for its property of fixing other odours. It is employed in pharmacy to disguise disagreeable odours, especially that of iodoform, for which purpose 1 part of coumarin is used to 50 parts of iodoform.

(1)

Coumarin and its derivatives occur naturally, both in the free state and as glycosides. Coumarins comprise a group of natural compounds found in a variety of plant sources.
They are especially abundant in grasses, orchids, legumes and citrus fruits. The parent compound coumarin is the sweet smelling constituent of white clover. Certain naturally occurring coumarins and their sources are listed in Table 1 given below.

### Table 1 Different sources of variety of coumarins

<table>
<thead>
<tr>
<th>Coumarins</th>
<th>Sources</th>
</tr>
</thead>
<tbody>
<tr>
<td>1. Ostenol, Arnotlinin and</td>
<td>Leaves, bark and wood of Zanthoxylum monophyllum (Rutaceae)</td>
</tr>
<tr>
<td>Columbranetin</td>
<td></td>
</tr>
<tr>
<td>2. Scopoletin, Angelol I,</td>
<td>Angelica dahurica</td>
</tr>
<tr>
<td>Angelol H</td>
<td></td>
</tr>
<tr>
<td>3. Melilotoside</td>
<td>Melilotus oederante, Melilotus altissima, Melilotus arvesis</td>
</tr>
<tr>
<td>4. Umbelliferone</td>
<td>Bark of the spurge laurel and from the dry distillation of resins from</td>
</tr>
<tr>
<td></td>
<td>some Umbellifera.</td>
</tr>
<tr>
<td>5. Herniaren</td>
<td>Herniaria hirsute</td>
</tr>
<tr>
<td>6. Skimming</td>
<td>Skimming japonica</td>
</tr>
<tr>
<td>7. Dicumarol</td>
<td>Spoiled hay or silage from the common sweet clover</td>
</tr>
<tr>
<td>8. Citropten</td>
<td>Citrus fruits, West Indian lime oil.</td>
</tr>
<tr>
<td>9. Esculetin and Esculin</td>
<td>Bark of horse chest nut</td>
</tr>
<tr>
<td>10. Scopolin</td>
<td>Root of Scopolia japonica</td>
</tr>
<tr>
<td>11. Cichoriin</td>
<td>Blossoms of the chicory</td>
</tr>
<tr>
<td>12. Ayapin</td>
<td>Leaves of Eupatorium ayapana Vent</td>
</tr>
<tr>
<td>13. Daphnetin, Daphnin and</td>
<td>Thymelacaceen, Daphne alpina</td>
</tr>
<tr>
<td>Fraxetin</td>
<td></td>
</tr>
</tbody>
</table>

The very long association of plant coumarins with various animal species and other organisms throughout evolution may account for the extraordinary range of biochemical and pharmacological activities of these chemicals in mammalian and other biological systems. Some naturally occurring coumarin derivatives include umbelliferone (7-hydroxycoumarin), aesculetin (6,7-dihydroxycoumarin), scopoletin (7-hydroxy-6-methoxycoumarin), psoralen and imperatorin. Synthetic 7-hydroxy coumarins are used to absorb ultraviolet rays in sunscreen.
cosmetics and used in the synthesis of drugs especially anticancer. Scopoletin is used as a peroxide or calcium signal during the oxidative burst. It is an acetylcholinesterase inhibitor.

Coumarin has clinical value as the precursor for several anti-coagulants, notably warfarin (2) that is administered orally or very rarely, by injection. Its derivatives found applications as antibiotic, anti-fungicidal, anti-microbial, anti-tumour agents and as HIV anti-proliferator. It increases the blood flow in the veins and decreases capillary permeability. The fluorescent nature of coumarin derivatives led to its wide spread use in industries as perfumery and fluorescent dyes. It is used for the prophylaxis of thrombosis and embolism in many disorders in which there is excessive or undesirable clotting, such as thrombophlebitis, pulmonary embolism, and certain cardiac conditions (Holbrook et al., 2005) Coumarin derivatives are also used as rodenticides due to the property of causing fatal hemorrhaging.

![Coumarin](image)

Umbelliforone (3) occurs in many familiar plants from the Apiaceae family such as carrot, coriander, garden angelica. The ultraviolet activity of umbelliforone leads to its use as a sunscreen agent and an optical brightener for textiles. It has also been used as gain medium for dye lasers (Barton et al., 1999). It can be used as a fluorescence indicator for metal ions such as copper and calcium.

![Umbelliforone](image)

4-Methylcoumarins (4) are implicated to have several beneficial pharmacological effects (Takeda and Aburada, 1981; Deana et al., 1983). A large number of 4-methylcoumarins and 4-methylthionocoumarins have antioxidant activity towards NADPH-catalysed liver-microsomal lipid peroxidation. Unsubstituted coumarins appear to be toxic because of their oxidative
decarboxylation, resulting in the formation of o-hydroxyphenylacetaldehyde or o-hydroxyphenylacetic acid derivatives which form very stable complexes with heavy metals inside the body (Lake, 1999). On the other hand, 4-methylcoumarins are reluctant towards oxidative decarboxylation and hence, are non-toxic.

\[ R^1 = \text{H/-OCH}_3/-\text{Ph/-C}_6\text{H}_4\text{Br} \]
\[ R^2, R^3, R^4, R^5 = \text{H/-OH/-OCH/-OCOCH/-Br} \]

(4)

Psoralen (5) is a parent compound in a family of natural products known as furcoumarin. It is structurally related to coumarin by the addition of a fused furan ring. Psoralen occurs naturally in the seeds of Psoralea Corylifolia. It is widely used in the treatment for psoriasis, eczema and vitiligo (Dewick, 2009).

(5)

Brodifacoum (6) is a highly lethal anticoagulant poison. It is widely used as azpesticides as well as rodenticide. A mixture of brodifacoum and marijuana prevents bleeding disorders (La Rosa et al., 1997). Imperatorin (7) is a furcoumarin. It is an active single derivative of Angelica dahurica, a Chinese herb and has anti-HIV effects as well as effects on abnormal heart muscle thickening (hypertrophy), but can also have some neurotoxic effects.

(6)  (7)
Dicumarol or 3,3-Methylenebis-(4-hydroxycoumarin) (8) is used orally as anticoagulant in the prophylaxis and treatment of antivascular clotting. It is also used in biochemical experiments as an inhibitor of reductases (Cullen et al., 2003). It is employed in postoperative thrombophlebitis, pulmonary embolus, acute embolic and thrombotic occlusion of peripheral arteries and recurrent idiopathic thrombophlebitis to arrest impending gangrene and frostbite.

\[
\text{(8)}
\]

Coumarin1 (9), Coumarin6 (10), Coumarin30 (11), Coumarin314 (12) and Coumarin343 (13) are some examples of fluorescent dyes all of which exhibit high fluorescent properties (Du et al., 1998).

\[
\text{(9)} \quad \text{(10)} \quad \text{(11)} \quad \text{(12)} \quad \text{(13)}
\]
Aminocoumarin dyes are widely used as fluorescent probes (Kumbhakar et al., 2006). For example coumarin500 (14) and coumarin151(15) have the properties of fluorescent probes to monitor changes in the micro environment in organized medium.

![Chemical structures of coumarin 500 (14) and coumarin 151 (15)](image)

Some coumarin dyes (16) among organic dyes possess high solar energy transfer efficiency in DSCs (Xiao et al., 2008).

![Chemical structure of coumarin 16](image)

Coumarins show quite diverse biological activity and in addition to their anticoagulant properties. To cite some examples novobiocin (17) is an antibacterial (Keith et al., 1994), holoxon (18) is an anthelminitic (Martin, 1993) and mereumallic acid (19) is a diuretic.

![Chemical structure of novobiocin (17)](image)

Coumarin-3-carboxylic acid (20) is a sedative and a hypnotic (Ellis, 1998). 3-methyl-4-hydroxycoumarin (21) shows an opposite behavior to dicoumarol and exhibits vitamin-K like activity.

![Chemical structures of coumarin 18 and 19](image)
Coumarin is the most widely prescribed antithrombotic in North America. It has anticoagulant activities. Recently, it is found that 3-substituted-4-hydroxycoumarin compound, phenprocoumon and analogous compounds have been identified as active non-peptidic HIV protease inhibitors (Richard et al., 1997, Kulkarni et al., 2006).

Apart from these biological activities, coumarin and its derivatives find extensive use as optical brightening agents in laundry and domestic detergents and additive to fibers and papers due to their absorption of UV light. Xanthenes and 7-aminocoumarins are the two very important classes of laser dyes. For example rhodamin (22) is a xanthene used as a laser dye. 7-Aminocoumarins (23 & 24) also exhibit excellent properties of a laser dye (Sokodowska et al., 2001).

Coumarin 521 (25) is used as fluorescence resonance energy transfer agent (Pavel and Manuel, 2009).
Polyphenolic compounds have drawn greater attention compared to any other class of natural products for their significant biological functions as antioxidants and anticarcinogens or antimutagens, which have led to their recognition as potential neutraceuticals. Among them, phenolics that include coumarins, xanthones, flavones, etc. have attracted considerable attention.

1.2 Methoxycoumarins

Another heteroyl moiety which we have got interest is 8-methoxycoumarin. Methoxycoumarins were reported to have many pharmacological and industrial applications (Rahman et al., 2001). The pharmacological, biochemical properties and therapeutic applications of simple coumarins depend upon their pattern of substitution.

Herniarin (7-methoxycoumarin) (26) is a naturally occurring coumarin. Herniarin is a methoxy analog of umbelliferone possessing anticoagulant properties. It can be found in Herniaria glabra and is one of the possible coumarin allergens in chamomile. Herniarin indeed is one of the non-sesquiterpene lactone sensitizers in German chamomile (Evy et al., 2010).

3-Bromoacetyl-7-methoxycoumarin (27) is useful as an additional highly reactive and a convenient fluorescent derivatization reagent for carboxylic acids in HPLC analysis (Akira et al., 1992).

Some coumarin derivatives are used as derivatization reagents for carboxylic acid in HPLC (Goya et al., 1981; Goya et al., 1982; Takedate et al., 1982). Various coumarins are reported as fluorescence derivatization reagents for high-performance liquid chromatographic analysis (Takedate et al., 1985; Takedate et al., 1989) and as fluorescence probes (28 a-d) for drug-protein binding studies (Takedate et al., 1995).
4-Bromomethyl-7-methoxycoumarin (29) is used as a derivatizing reagent for fatty acids and this compound in the presence of analogous catalysts in aqueous micellar systems also possesses derivatization character (Van der Horst et al., 1988; Van der Horst et al., 1990).

7-Methoxycoumarin-4-acetic acid (30) and 7-Methoxycoumarin-3-carboxylic acid (31) is very effective as fluorescent dyes.

Some methoxy derivatives naturally occurring in plants are 8-acetyl-7-hydroxy-6-methoxycoumarin (32) and 8-methoxycoumarin (Nagarajan et al., 1980) in *Fraxinus floribunda* leaves, trigoforin (3,4,7-trimethylcoumarin) (Khurana et al., 1982) in *Trigonella foenumgraecum* stems, troupin (4-methyl-6-hydroxy-7,8-dimethoxycoumarin) (Parmar et al., 1985) and trigocoumarin (3-(ethoxycarbonyl)methyl-4-methyl-5,8-dimethoxycoumarin) (Parmar et al., 1981) in *Tamarix troupii* and *Trigonella foenumgraecum*, respectively. These naturally occurring coumarins are effective NADPH inhibitors and found use as anti-oxidant compounds.
1.3 Benzothiazole

Benzothiazoles are a group of xenobiotic, heterocyclic chemicals which contain a benzene ring fused with a thiazole ring. The benzothiazole moiety is present in various natural and synthetic compounds with numerous pharmaceutical and industrial applications. Benzothiazole derivatives have diverse biological applications such as antifungal, antibacterial, antiinflammatory, antiallergic, antitumor, local anesthetic, cytotoxic and inhibition of some enzyme activities.

Benzothiazole (33) has been seen in aroma fraction of tea leaves, cow’s milk, flavour compound produced by the fungi Polyporous Frondosus and Aspergillus Clavatus. Further more they are present in the volatile fraction of oak wood used for aging wines (Vincenzo et al., 2000).

Benzothiazoles have wide range of practical applications as antioxidants, as vulcanization accelerator, in UV and thermal stabilizers for polymer materials, in dyes and diazotype materials in electro photography and in analytical chemistry for their chelating properties. They have also been studied for use in photodegradation of poly vinyl chloride (PVC) photosensitizers.

(33)

2(2-pyridyl)benzothiazoles (Katayoun et al., 2009) known as PBT has gained special attention for its use in electroluminescent devices because of its structural and physico chemical properties. PBT is reported as an effective corrosion inhibitor for low carbon steel in acidic media. As biological active compounds, platinum complexes of PBT are candidates for replacing cisplatin with more effective drug that can be administrated orally and with reduced side effects. Re and Te complexes of PBT serve as preliminary models for the development of radiopharmaceuticals for tumor imaging and/or radio therapy as well as diagnosis for Alzheimer’s disease.
Benzothiazoles are used in a variety of industrial products and processes. Benzothiazole based thiazole chemicals are widely used in the rubber industry due to their excellent stability, functionality and low cost. Over 90% of all usage is as cure-rate accelerators in the manufacture of tyres (side wall, tread and retread carcass, belt skim, liner, bead filler/chafer and base tread) and industrial rubber products (automotive extruded sponge latex and insulated wire, insulation jackets, molded and mechanical goods).

2-Mercaptobenzothiazole (34) is a rubber additive chemical (e.g. vulcanization accelerator) (Katritzky et al., 1995) used as a corrosive inhibitor and fungicide, while 4-morphinyl-2-benzothiazole disulphide (35) is a very important vulcanizer that can provide sulfur for cross linking.

4-Methyl-1,3-benzothiazol-2-pyridine-2-hydrazone (36) can be used as a suitable neutral ionophore for preparing an Er(111) membrane sensor with high selectivity (Mohammad et al., 2007).

Benzothiazole derivatives such as (37) and (38) are used as diode laser compatible fluoprobes and find application in high technology areas of biotechnology such as immune assay, single molecule detection and protein labeling (Bernhard and Michaela et al., 2001).
4-Chloro-2-oxobenzothiazolin-3-yl-ethanoic acid (39) which is known as benazoline is used as an ingredient of herbicides.

2-(4-Aminophenyl)benzothiazole and its analogue (40) comprise a novel mechanistic class of antitumor agents. These compounds in nano molecular range elicit potent growth inhibition in human-derived breast, colon, ovarian and renal tumour cell lines. These agents have the potent selective activity mainly towards MCF-7 cells (Raghvendra et al., 2006).

Fluorinated 2-(4-aminophenyl)benzothiazoles are potent cyclotoxic agents which are able to block metabolic inactivation of benzothiazoles to inactive metabolite. Substitution of fluro group at 5- and 7- result in active compound towards sensitive cell lines while 4- and 6- fluro analogues are inactive towards sensitive cell lines (Hutchinson et al., 2001).

Thioflavine (41) is a benzothiazole derivative which is used to visualize plaques composed of amyloid beta found in the brains of Alzheimer’s disease patients (Wei et al., 2005).
Benzothiazolylthiourea presents mast cell inhibitory activity, which is important in the treatment of asthma. 1-Aroyl-3-(substitutedbenzothiazolyl)thiourea (42) exhibit moderate to potent activity towards the tested micro organisms as compared to standard drugs (Saeed et al., 2008).

![Chemical structure of 1-Aroyl-3-(substitutedbenzothiazolyl)thiourea (42)](image)

2-[(2-Chlorobenzothiazol-6-yl)amino]benzoic acid (43) demonstrates an interesting antiproliferative activity towards the parasite of the species Trichomonas Vagilantis while 2-[(2-hydroxyethyl)amino]benzothiazol-6-yl]amino)benzoic acid exhibit a promising activity against the parasite of the species Leishmania infantum in their amastigote form (Sawhney et al., 1974).

![Chemical structure of 2-[(2-Chlorobenzothiazol-6-yl)amino]benzoic acid (43)](image)

6-Trifluromethoxy-2-ben zothiazolamine (44) which is known as riluzole was found to interfere with glutamate neuro transmission in biochemical, electrophysiological and behavioral experiments. It is used as a drug to treat amyotrophic lateral sclerosis (Mathew et al., 2005)

![Chemical structure of 6-Trifluromethoxy-2-ben zothiazolamine (44)](image)

2-(3,4-Dimethoxyphenyl)-5-flurobenzothiazole (45) is considered as a potent ligand for the aryl hydrocarbon receptor which translocate with the drug to cell nuclei (Yaseen et al., 2008).

![Chemical structure of 2-(3,4-Dimethoxyphenyl)-5-flurobenzothiazole (45)](image)

The benzothiazole anthelimitic, methyl-6-propoxybenzothiazol-2-carbamate (tioxidazole, TIOX.), was reported to exert its chemotherapeutic action on Hymenolepis diminuta by decreasing the ability of the worm to absorb and metabolize exogenous glucose (Mona et al., 2007).
The dihydrochloride salt of the lysylamide prodrug of 2-(4-amino-3-methylphenyl)-5-fluorobenzothiazole (5F 203) (46) is an experimental antitumor agent with potent and selective activity against human-derived carcinomas of breast, ovarian and renal origin (Iduna et al., 2004).

![Image](image)

Amberlite IR120 (47) chemically known as dibenzothiazole disulphide is used as resin in kinetic reactions.

![Image](image)

2-Aminobenzothiazole (48) is used as a relaxant (Arpana et al., 2007).

![Image](image)

Primuline (http://en.wikipedia.org/wiki/Primuline) (49) is a fluorescent dye containing benzothiazole moiety. This is a dye which gives yellow colour to cotton without the aid of any mordents.

![Image](image)

The benzothiazole derivative (50) exhibit antiviral, antimicrobial, anti mycobacterial and antiproliferative activity.

![Image](image)

Hydroxyoxodihydrobenzothiazole derivatives such as (51) are used as B2-adrenoreceptor modulators (Connolly et al., 2008).
Benzothiazoles are used as slimicides in the paper industry. They are also used as fungicides and as herbicides or as anti-algal agents. Benzothiazoles are used in a variety of industrial products and processes, thus it is commonly found in the aquatic environment (Vincenzo et al., 2000). Model compounds containing the benzothiazole unit have much interest for their optical properties. They have also been used as organic luminophores. The interesting and often unusual photochemical and photo physical properties of these compounds are attributed to the presence of two different chromophores in their molecules namely the benzothiazole moiety and the substituted aromatic ring.

1.4 Thiazole

Thiazole (52) is a 5-membered ring, in which two of the vertices of the ring are nitrogen and sulfur, and the other three are carbons, has been of much interest to chemists and pharmacologists because of its industrial and biological importance (Jalal et al., 1989; Katritzky et al., 1995). Thiazole is a very stable molecule, it's uses include analgesic, anaesthetic, antiallergic, anti-inflammatory, immunoregulatory, blood cholesterol lowering, anthelmintic, antitussive, antitumour, antitubercular, antiarthritic, immunosuppressive, psychoactive and several other activities(Jalal et al., 1989; Katritzky et al., 1995). It is a parent material for numerous chemical compounds including sulfur drugs, biocides, fungicides, dyes and chemical reaction accelerators. Thiazole dyes contain the color radicals of =C=N- and -S-C= which decide colors to a compound. Thiazole dyes are useful in dying cotton.
2-Aminothiazole (53) is a heterocyclic amine with odor similar to pyridine, soluble in water, alcohol and ether. 2-Aminothiazole can be used as a thyroid inhibitor in the treatment of hyperthyroidism and it has antibacterial activity (Thomas, 1976). Aminothiazole is an intermediate for dyestuffs, photographic chemicals and pharmaceuticals (example: as a side chain of Cephalosprins). A derivative of 2-aminothiazole namely, 2-aminothiazol-4-carboxylic amides is used as protein kinase inhibitors (Gerald et al., 2010).

A very important derivative of thiazole is sulfathiazole (54) which is used in the treatment of inflections due to Pneumococcus and Staphylococcus aureus.

Phthalysulfathiazole (55) is a sulphonamide used as an intestinal antibacterial agent and is used in the treatment of bacillary dysentery. Succinyl sulfathiazole (56) is also an antibacterial agent. Due to its slow adsorption and low toxicity, it is useful in bacillary dysentery and cholera.
The 4-aminothiazol-2-thione (57) possesses antifungal activity and 4-chloro-2-oxobenzothiazolin-3-ylacetic acid (58) is used as an ingredient of herbicides.

![Chemical Structure of 4-aminothiazol-2-thione (57) and 4-chloro-2-oxobenzothiazolin-3-ylacetic acid (58)]

Thiabendazole (59), substituted derivative of benzimidazole, is used as broad-spectrum anthelmintic and preservative (Dalvie et al., 2006). Some thiazole derivatives belong to a class of cyclic sulfur organo products containing sulfur atom (S) and often oxygen (O), nitrogen (N), hydrogen (H), as well as other elements, can find application for making biologically active agents such as antiviral, antibacterial, antifungal, antituberculous, antibody and antifungal agents. Thiazole and its derivatives are also used as thiol flavouring substances.

![Chemical Structure of Thiabendazole (59)]

Thiazofurin (60) with an amide group as the 4-substituent, is a thiazole derivative with antitumour activity against human leukemic cells (Jayaram et al., 1986). Ceftriaxone (61) also known as Rocephin is a synthetic antibiotic containing a 4-substituted-2-aminothiazole ring (Bradley et al., 2009). Ceftriaxone is often used (in combination, but not direct, with macrolide and/or aminoglycoside antibiotics) for the treatment of community-acquired pneumonia. It is also a choice drug for treatment of bacterial meningitis.

![Chemical Structure of Thiazofurin (60) and Ceftriaxone (61)]

$N$-(Cyano-2-thienylmethyl)-4-ethyl-2-(ethylamino)-5-thiazolecarboxamide
(63) commonly known as ethaboxam, is a systemic fungicide which is taken into the plant and transported through the xylem following application to the soil. It is also transported translaminarly (Kim et al., 2004).

\[
\begin{array}{c}
\text{H}_3\text{C} - \text{N} - \text{S} - \text{N} - \text{CH}_2 - \text{O} \\
\text{H} - \text{S} - \text{N} - \text{C} \text{N} - \text{S}
\end{array}
\]

(63)

Thiochrome (64) is a yellow strongly fluorescent pigment.

\[
\begin{array}{c}
\text{H}_3\text{C} - \text{N} - \text{S} - \text{N} - \text{S} - \text{HC} = \text{CH} - \text{OH} \\
\text{CH}_3
\end{array}
\]

(64)

The thiazole unit is also found in naturally occurring bioactive substances. For example vitamin B (thiamine) contains this ring. Luciferin (65) is a natural bioluminescent agent of fireflies that contains a benzothiazole moiety (Hastings, 1996). Some of the other compounds which incorporate thiazole ring system are the unusual \(\alpha\)-amino acid (66) with a benzofused moiety is present in the pigment of bird feathers.

\[
\begin{array}{c}
\text{HO} - \text{S} - \text{N} - \text{C} \text{H}_2 \text{O} - \text{COOH}
\end{array}
\]

(65)

\[
\begin{array}{c}
\text{H}_2\text{C} - \text{CH} - \text{CH} - \text{NH} - \text{COOH}
\end{array}
\]

(66)

A large number of flavors and aromas of food contains thiazoles nucleus or its simple derivatives for example 4-methyl-5-vinylthiazole (67) is present in cocoa.

\[
\begin{array}{c}
\text{H}_3\text{C} - \text{C} = \text{CH} - \text{S} - \text{N}
\end{array}
\]

(67)

A marine natural product containing thiazole ring is anguibactin (68) which is a siderophore and has been isolated from a marine pathogen.
Aztreonam (69) is a synthetic monocyclic beta-lactam antibiotic originally isolated from *Chromobacterium violaceum*. Aztreonam is similar in action to penicillin. It inhibits mucopeptide synthesis in the bacterial cell wall. It is known to be effective against a wide range of bacteria including *Citrobacter, Enterobacter, E coli, Haemophilus, Klebsiella, Proteus*, and *Serratia* species (Kobayashi et al., 1992).

Cefdinir (70) is a semi-synthetic, broad-spectrum antibiotic in the third generation of the cephalosporin class, proven effective for common bacterial infections of the ear, sinus, throat, and skin. Therapeutic uses of cefdinir include otitis media, soft tissue infections, and respiratory tract infections, including sinusitis, strep throat, community-acquired pneumonia and acute exacerbations of bronchitis (http://en.wikipedia.org).

Cefixime (71) is an oral third generation cephalosporin antibiotic, used to treat gonorrhea (McMillan and Young et al., 2007). Cefmenoxime (72) is another third generation cephalosporin antibiotic (Yokota et al., 1995).
Clomethiazole (73) is a sedative and hypnotic that is widely used in treating and preventing symptoms of acute alcohol withdrawal. It is a drug which is structurally related to thiamine (vitamin B1) but acts like a sedative, hypnotic, muscle relaxant and anticonvulsant. It is also used for the management of agitation, restlessness, short-term insomnia and Parkinson's disease in the elderly (Reith, 2003).

Dasatinib (74) is an oral dual BCR/ABL and Src family tyrosine kinases inhibitor approved for use in patients with chronic myelogenous leukemia (CML) after imatinib treatment and Philadelphia chromosome-positive acute lymphoblastic leukemia (Ph+ ALL). It is also being assessed for use in metastatic melanoma (Talpaz et al., 2006).

The epothilones (75) are a new class of cytotoxic molecules, including epothilone A, epothilone B, and epothilone D, identified as potential chemotherapy drugs. The principal mechanism of the epothilone class is inhibition of microtubule function. Microtubules are essential to cell division, and epothilones therefore stop cells from properly dividing (Luduvico et al., 2006).
Ethoxzolamide (76) is a sulfonamide medication that functions as a carbonic anhydrase inhibitor. It is used in the treatment of glaucoma, duodenal ulcers, and as a diuretic. It may also be used in the treatment of some forms of epilepsy.

Meloxicam (77) is a nonsteroidal anti-inflammatory drug used to relieve the symptoms of arthritis, primary dysmenorrhea and fever; and as an analgesic, especially where there is an inflammatory component. Meloxicam significantly decreased symptoms of pain, function, and stiffness in patients, with a low incidence of gastrointestinal side effects (Engelhardt, 1995).

Nitazoxanide (78) is a synthetic nitrothiazolyl-salicylamide derivative and an anti-protozoal agent. It is approved for treatment of infectious diarrhea caused by *Cryptosporidium parvum* and *Giardia lamblia* in patients 1 year of age and older. Following oral administration it is rapidly hydrolyzed to its active metabolite, tizoxanide, which is 99% protein bound. Peak concentrations are observed 1–4 hours after administration. It is excreted in the urine, bile and faeces. Untoward effects include abdominal pain, vomiting and diarrhea (Vanessa et al., 2007).
Nizatidine (79) is a histamine H2-receptor antagonist that inhibits stomach acid production, and commonly used in the treatment of peptic ulcer disease (PUD) and gastroesophageal reflux disease (GERD) (Atmaca et al., 2004).

Vitachrome (80) is an intensely blue fluorescing substance containing two thiazole rings.

Indanthrene yellow (81) is a thiazole dye which has excellent fastness (Freeman and Mock, 2007).

Algol yellow GC (82) is a dithiazole anthraquinone dye (Louis and Mary, 1944) which contains thiazole ring.

Triheterocyclic thiazoles containing coumarin (83) are reported to have in vivo analgesic and anti-inflammatory activities (Kalkhambkar et al., 2007). Number of 2,4-disubstituted thiazoles,
imidazolyl thiazoles, and pyrazolyl thiazoles have been recognized as potent anti-inflammatory and analgesic agents (Shivarama et al., 2003; Sharma and Sawhney, 1997; Russo et al., 1993; Kulkarni et al., 1981). Synthesis of many 3-substituted biheterocyclic coumarins with thiazoles and fused thiazoles possessing antimicrobial and anti-inflammatory agents has been reported (Kulkarni et al., 1990; Pettit et al., 1987).

Molecules incorporating one or more thiazole unit in their system are found to possess a wide range of biological activity. For example, dolastatins (Arabshahi and Schmitz, 1988) which are naturally occurring cyclic peptides containing thiazole ring are highly potent antineoplastic agents and ulithiacyclamide is a good naturally occurring drug against leukemia. Three new thiazole containing macrocyclics are petellamides D, E and ulithyacyclamide B are thiazoles of marine origin with excellent anticancer activity.

The above summary on the various reported uses of the different heterocyclic compounds amply demonstrate the wide application of compounds belonging to these heterocyclic families. Several methods have been reported for the synthesis of coumarins, benzothiazoles and thiazoles. Among these, the one pertaining to the preparation of coumarins/ benzothiazoles with attention to 3-ketocoumarin/ 3-ketobenzothiazole and 5-substituted thiazoles with special emphasis to 2-amino-5-ketothiazoles alone is reviewed in the next chapter.