CHAPTER II

MATERIALS AND METHODS

The details regarding the materials used for the present investigation and the procedures adopted for the preparation of the 'samples' are briefly outlined. Introduction to thermal analysis, brief descriptions of important thermal analysis methods, various types of methods used for the kinetics and mechanism of thermal decomposition reactions from TG data are also given. A brief account of the mineral metabolism and the biological importance of the metal ions used for the present investigation are also included.
2.1 Materials

The details of the materials used for the present investigation are given as follows. The five carbohydrates chosen for the present investigation are two monosaccharides, *viz.*, glucose and fructose, and three disaccharides, *viz.*, lactose, maltose and sucrose. Anhydrous samples of glucose, fructose and sucrose, and monohydrates of lactose and maltose (AnalaR grade Merck samples) were purchased and used as such without further purification.

The metal salts used include the chlorides of Na(I), K(I), Ba(II), Mg(II), Ca(II), Mn(II), Fe(III), Co(II), Ni(II), Cu(II), Zn(II) and Sn(II). Thus, the following twelve AnalaR grade Merck samples of NaCl (anhydrous), KCl (anhydrous), BaCl₂₂H₂O, MgCl₂.6H₂O, CaCl₂₂H₂O, MnCl₂.4H₂O, FeCl₃ (anhydrous), CoCl₂.6H₂O, NiCl₂.6H₂O, CuCl₂₂H₂O, ZnCl₂ (anhydrous) and SnCl₂ (anhydrous) were also purchased and used as such without further purification.

2.2 Preparation of the samples for TG studies

All the five carbohydrates, *viz.*, glucose, fructose, lactose, maltose and sucrose were finely powdered, sieved through a 230 mesh sieve and dried *in vacuo* over phosphorus(V) oxide. Glucose samples containing 1%, 5% and 10% (W/W) each of the twelve metal chlorides were prepared. Fructose, sucrose, maltose and lactose samples containing 5% (W/W) metal chloride were also prepared with all the twelve metal chlorides. These metal doped samples of four of the carbohydrates excluding fructose were prepared by a common procedure as described. Stock solutions (1% W/V) of all the five carbohydrates and twelve metal chlorides were prepared in water. Solution of each of the carbohydrates and that of each of the metal chlorides were mixed together in the required proportion as given above. The resulting solution was kept at 40°C and subjected to mechanical shaking for 2 h. Then the solution was evaporated to dryness on a water bath set at 60°C. The resulting residue obtained in each case was finely powdered, sieved through a 230 mesh sieve and dried *in vacuo* over phosphorus(V) oxide.
Since the fructose has very high affinity for water, the above described wet method could not be successful for the preparation of the metal doped fructose samples. Therefore, a dry method was adopted for the preparation of fructose samples. Thus, finely powdered fructose and each of the twelve metal chlorides were mixed together in the required proportion to get samples having 5% (W/W) metal chloride using an agate mortar and pestle. The resulting mixture was made into a solid solution by uniform mixing for 2 h. The samples so prepared were sieved through a 230 mesh sieve and dried in vacuo over phosphorus(V) oxide.

2.3 Thermal analysis of the samples

A known amount of each the samples prepared (~3 mg) was taken for thermogravimetric studies. The TG, DTG and DTA curves of all the samples were recorded on a Mettler Toledo STARe thermal analysis system consisting of the STARe software and the TGS/SDTA 851e module. A linear heating rate of 10°C min⁻¹ in an atmosphere of dynamic air (flow rate, 60 mL min⁻¹) was used for all the TG measurements in the temperature range of 30 - 800°C. The data obtained from the TG/DTG/DTA curves were used for the detailed studies of the thermal behaviour of these samples. The kinetics and mechanisms of thermal decomposition reactions of all the samples were also studied using the TG data. The kinetic parameters such as order parameter (n), activation energy (E), pre-exponential factor (A) and entropy of activation (ΔS) have been calculated.

2.4 The mineral metabolism

Minerals are the constituents, which remain as ash after the incineration of plant and animal tissues. Minerals perform several vital functions, which are absolutely essential for the very existence of the organism. These include calcification of bone, blood coagulation, neuromuscular irritability, acid-base equilibrium, fluid balance and osmotic regulation.
2.5 Classification of minerals

Minerals are classified as principal elements or main elements and trace elements. The seven principal elements constitute 60 - 80% of the body's inorganic materials, which are calcium, magnesium, sodium, potassium, chlorine, phosphorus and sulphur. The trace elements are subdivided into following three categories.

a) Essential trace elements: chromium, cobalt, copper, iron, manganese, molybdenum, selenium, zinc and fluorine

b) Possibly essential trace elements: barium, cadmium, nickel and vanadium

c) Non-essential trace elements: aluminium, bismuth, boron, lead, mercury and silver

The mineral contents of human body may be summarized as follows. Calcium constitutes 10-20 g/kg of human body, phosphorus 6 - 12 g/kg, potassium 2 - 2.5 g/kg, sodium 1 - 1.5 g/kg, chloride 1 - 1.2 g/kg, magnesium 0.4 - 0.5 g/kg, iron 70 - 100 mg/kg, zinc 20 - 30 mg/kg, copper 1.5 - 2.5 mg/kg, manganese 0.15 - 0.3 mg/kg, iodine 0.1 - 0.2 mg/kg and molybdenum 0.1 mg/kg.

2.6 Minerals used in the present investigation

The present investigation involves the thermal analysis of carbohydrates such as glucose, fructose, sucrose, maltose and lactose doped with specified quantities of NaCl, KCl, MgCl₂, CaCl₂, BaCl₂, MnCl₂, FeCl₃, CoCl₂, NiCl₂, CuCl₂, ZnCl₂ and SnCl₂. The biological importance of the metal ions used are briefly discussed below.

2.6.1 Sodium

Sodium ion, Na⁺ is the chief cation in the extra cellular fluid. About 50% of sodium is present in the bones, 40% in the extra cellular fluid and remaining
10% in the soft tissues. The Na⁺ content of the body is 1.4g/kg. The adults' minimum requirement of Na⁺ averages from 460 mg/day. There are several biochemical functions of sodium. In association with chloride and bicarbonate, sodium regulates the body's acid-base balance. Sodium is required for the maintenance of osmotic pressure and fluid balance. It is necessary for the normal muscle irritability and cell permeability. Sodium is involved in the intestinal absorption of glucose, galactose and amino acids. Na⁺ is necessary for initiating and maintaining heart beat. In the human cells there is an exchange of Ca²⁺ and Na⁺ ion along the plasma membrane due to the potential gradient. Ca²⁺ ion moves from the intracellular to extracellular sites and Na⁺ in the reverse direction. The study of this exchange in heart plasma membrane vesicles were conducted and reported that the ratio of Na⁺/Ca²⁺ should be 3:1. Sodium is extracted from the body through kidney. As much as 800g Na⁺/day is filtered by glomeruli, 99% of this is reabsorbed by the renal tubules by an active process. This is controlled by aldosterone. The increase and decrease in the level of Na⁺ in the body causes diseases. Hyponatremia is a condition, in which the sodium level falls below the normal. Hyponatremia may occur due to diarrhea, vomiting, chronic renal adrenocortical insufficiency (addison's disease). Decreased serum sodium concentration is also observed in edema, which occurs in cirrhosis or congestive heart failure. Hypernatremia is characterised by an elevation in the serum sodium level. It may occur due to hyperactivity of adrenal cortex.

2.6.2 Potassium

Potassium ion is the principal intracellular cation. It is equally important in the extracellular fluid for specific functions. The concentration of K⁺ in the body is 2g/kg. The minimum daily requirement of K⁺ in an adult is estimated to be 782 mg. Potassium maintains the intracellular osmotic pressure. The cells pump Na⁺ out of cytoplasm and K⁺ in to the cytoplasm. It is this difference in total alkali metal ion concentration inside and outside cells that produce an electrical potential across the cell membrane. The potential difference underlies many basic processes such as the hearts generation of rhythmic electrical signals, the kidney’s unceasing separation of vital and toxic solutes in blood, and the eye’s
precise control of lens' refractive index\textsuperscript{34}. Most of the power (10W) produced by the human brain-awake or asleep results from the Na\textsuperscript{+}/K\textsuperscript{+} adenosine triphosphate enzyme pumping potassium ions in to and sodium ions out of brain cells\textsuperscript{34}. When 'we go into shock' as a result of an accident, it is the massive leakage of the alkali metal ion through the cell walls that causes the phenomenon. K\textsuperscript{+} is required for the regulation of acid-base balance and water balance in the cell, for the transition of nerve-impulses, for the proper biosyntheses of proteins by ribosomes\textsuperscript{30}. The enzyme, pyruvatekinase (of glycolysis) is dependent on K\textsuperscript{+} for optimal activity. There are certain organic molecules, which are 'ion selective' due to the special architecture, and they are generally called 'ionophores'. Valinomycin is an example of such an ionophore. Valinomycin is used as a drug to transport potassium ion selectively across biological membranes. This effect in the mitochondria, K\textsuperscript{+} transport has been established\textsuperscript{35, 36}.

The deviation of the concentration of K\textsuperscript{+} ion in the cytoplasm from normalcy causes diseases. Hypokalemia or decrease in concentration of serum potassium is observed due to over activity of adrenal cortex (cushing's syndrome)\textsuperscript{30}. The symptoms of hypokalemia include irritability, muscular weakness and cardiac arrest. Hyperkalemia is the increase in concentration of serum potassium due to adrinocortical insufficiency (addison's disease). The manifestations of hyperkalemia include depression of central nervous system, mental confusion, numbeness, bradycardia with reduced heart sounds and, finally, cardiac arrest\textsuperscript{30}.

2.6.3 Magnesium

The adult body contains about 20 g of magnesium, 70% of which is bound in bones in combination with calcium and phosphorus. The remaining 30% of the total magnesium content occurs in the soft-tissues and body fluids\textsuperscript{30}. The adult man requires 350mg/day and adult woman requires 300mg/day. As a consequent and activator of many enzymes, particularly those associated with the conservation of energy-rich phosphate compounds and a stabilizer of plasma membranes, intracellular membranes and nucleic acids, magnesium is a life supporting element\textsuperscript{31}. Magnesium plays a very important role in the enzymatic
activity of human body. Magnesium is an activator for more than 300 enzymes and has a critical role in the transfer, storage and utilization of energy. Magnesium is sometimes involved in hydrolytic reactions. This is common when phosphate groups are involved, probably because the affinity of Mg\(^{2+}\) for phosphate group is high. The predominant role of magnesium is as an activator of phosphate transfer of organic phosphate groups, particularly reaction involving ATP. Magnesium has a pivotal role in carbohydrate, fat and protein metabolism. The Li\(^+\) ion is competing for the sites of Mg\(^{2+}\) in Mg-dependent enzymes. A number of studies in the biological systems due to this effect have been carried out.

The physiology of calcium and magnesium is directed towards a number of different functions, structural, signalling and regulatory. The cellular activities are controlled by their simple chemistry and osmotic reactions, which in turn, affect the way in which the body utilizes these metals. Regulations of these two elements take place to some extend reciprocally, although the exact mechanisms of magnesium’s regulation have not been fully established. The function of Mg\(^{2+}\) ions in polymerization of DNA molecules appears to involve binding the deoxynucleoside triphosphates to the enzyme. The Mg\(^{2+}\) is frequently used for in vitro protein synthesis.

### 2.6.4 Calcium

The total amount of calcium in the body is about 1,500 g. Calcium is considered as an essential nutrient because of its importance in building and maintaining bones, teeth and other biological functions. In human, the blood plasma level of total calcium is kept constant (≈ 2.45 mM) within narrow limits. On a cellular level the cytoplasmic Ca\(^{2+}\) concentration at least in eucaryotic cells, is very low, in the order of 100 nM. At the same time the concentration of Ca\(^{2+}\) in certain organelles, such as endoplasmic reticulum or mitochondria may be considerably high. In human, the uptake of Ca\(^{2+}\) from food occurs in small intestine, and transport is regulated by a metabolite of vitamin D, calcitriol (1,2,5-dihydroxy vitamin D\(_3\)). To maintain homeostasis and keep the calcium...
level in blood plasma constant, excess calcium is excreted through the kidney. The main factor controlling this phenomenon in vertebrates is the level of the parathyroid hormone that acts on kidney (increases Ca\(^{2+}\) resorption), on bone, and indirectly stimulated production of calcitriol, on the intestinal tract (increases Ca\(^{2+}\) uptake). Calcium enters the cell from the intestinal lumen by travelling through the brush-border membrane of the intestinal epithelial cell. Transfer through the brush-border membrane is assumed to be “passive”, although indirectly facilitated by calcitriol. The calcitriol effect may be due the synthesis of carrier protein\(^{48}\), but could also be an effect of altered membrane lipid composition\(^ {49}\).

There are some apparent analogies between intestinal Ca\(^{2+}\) transport and that occurring in placenta. Transplacental movement of Ca\(^{2+}\) increases dramatically during the last trimester gestation\(^ {50}\). The protein synthesis in this tissue appears to be under calcitrol regulation\(^ {32}\). The Ca\(^{2+}\) ions have to be supplied by the mammalian females, not only to the fetus during pregnancy, but also to the new born child through mother’s milk. In milk, Ca\(^{2+}\) is bound mainly to micelles of casein, and the average Ca\(^{2+}\) content is reported to be 2.5 g/L\(^ {32}\).

Calcium along with phosphate is required for the formation of bone and teeth. The bone is continuously remodelled and dissolved. The loss of bone mass in human occurring with increasing age makes bone susceptible to breaking under stress. The osteoblast cells handle bone formation and osteoclast cells make to erode\(^ {32}\). It is estimated that 5 to 10 percent of bone in an adult mammal is replaced per-year\(^ {51}\) due to the above two phenomena.

Calcium plays an important role in the muscular contraction. Calcium interacts with troponin C to trigger muscle contraction. Troponin C is the calcium binding subunit of troponin. The skeletal muscle troponin C, and cardiac-muscle troponin C are of slight different structures. The conformational changes taking place during muscular contraction and the mechanism have been studied\(^ {52-54}\). The Ca\(^{2+}\) is necessary for the transmission of nerve impulses\(^ {48,55-56}\). It has the messenger function. A transitory increase in intracellular Ca\(^{2+}\) concentration is observed in response to the binding of a hormone by an extracellular Ca\(^{2+}\) ions\(^ {57-59}\). Here, Ca\(^{2+}\) acts as a second messenger. Receptors for this
messenger have been found in the membranes of intracellular organells, and binding of 1, 4, 5-IP\textsubscript{3} to these receptors results in the release of Ca\textsuperscript{2+} ions\textsuperscript{60}. The Ca\textsuperscript{2+} has enzymatic activity. Proton kinase C is an example of a Ca\textsuperscript{2+} with enzymatic activity. Its activity increases in presence of Ca\textsuperscript{2+}, and it has a high calcium-binding constant in presence of phorbol esters\textsuperscript{61}.

The mammary glands produce, among other substances, a Ca\textsuperscript{2+}-binding enzyme activator, α-lactalbumin, that has about 40% sequence identity with lysozome\textsuperscript{32}. This protein, which is involved in the conversion of glucose into lactose, is secreted in large quantities, and in human milk constitutes some 15% of total protein. The Ca\textsuperscript{2+} binding constant of bovine or human α-lactalbumin is in the order of 10\textsuperscript{7} M\textsuperscript{-1} under physiological conditions. The X-ray structure of α-lactalbumin from baboon milk has been determined to a high resolution\textsuperscript{62}. The blood clotting proceeds in a complicated cascade of linked events involving many enzymes and proenzymes, where Ca\textsuperscript{2+} ion binding has also been operated. The most studied γ-carboxyglutamic acid (Gla) protein in the blood-clotting system is prothrombin. The Ca\textsuperscript{2+} binding studies of prothrombin and its fragments (proteolytic fragment-FI) have been conducted\textsuperscript{63, 64}. In presence of Ca\textsuperscript{2+} ions prothrombin and other vitamin-K-dependent proteins in blood coagulation system will bind to cell membranes containing acidic phospholipids, in particular, the platelet membranes which are rich in phatidylserine\textsuperscript{32}. The Ca\textsuperscript{2+} ions are involved in cell-to-cell and cell-to-extracellular matrix interactions, the molecular details are revealed by studies on thrombospondin\textsuperscript{65}. Each thrombospondin molecule is reported to bind 12 calcium ions with affinity of about 10\textsuperscript{4} M\textsuperscript{-1} and the removal of calcium is accompanied by a conformational change\textsuperscript{66, 67}.

2.6.5 Barium

Barium is an ultratrace element present in the body in micro minute amount. The biological effect of barium is still to be identified\textsuperscript{38}. However, it is a poisonous element, if the quantity increases. But the barium salt is used to take X-ray photographs of stomach and intestine. The element in the soft tissues does not absorb X-rays. Since barium ion is a good X-ray absorber, swallowing a
solution containing barium should be an obvious way of imaging these organs. For this purpose barium sulphate is made use of utilizing its extremely low solubility. Otherwise, the absorption of soluble barium ions by intestine will be poisonous. The slurry in water can be safely swallowed. The organ X-rayed and the compound later excreted.

2.6.6 Manganese

The total body content of manganese is about 15 mg. Liver and kidney are rich in manganese. Within the cells, manganese is mainly found in the nuclei in association with nucleic acids\textsuperscript{30}. The daily requirement is about 2 - 48 mg\textsuperscript{31}. Manganese serves as a co-factor for several enzymes. These include arginase, pyruvate carboxylase and isocitrate dehydrogenase. Manganese plays a critical role in oxygen evolution catalyzed by the proteins of photosynthetic reaction centre\textsuperscript{32}. The superoxide dismutase of bacteria and mitochondria, as well as pyruvate carboxylase in mammals are also manganese proteins\textsuperscript{68, 69}. Manganese is required for the formation of bone, proper reproduction and normal functioning of nervous system. Manganese is necessary for the synthesis of mucopolysaccharides and glycoproteins. Hemoglobin synthesis involves manganese. Manganese is necessary for cholesterol biosynthesis. Manganese in the serum is bound to a specific carrier protein-transmagnanin (a $\beta$-globulin). Manganese deficiency in animals causes retarded growth, bone deformities, accumulation of fat in liver, diminished activity of $\beta$-cells of pancreas (low insulin) and increased activity of serum alkaline-phosphates\textsuperscript{30}. The Mn(II) based superoxide dismutase (SOD) mimics of Zn Cu SOD enzyme were prepared. The Mn(II) mimics have numerous advantages over the SOD enzymes as potential therapeutic agents, including membrane permeability, selective reactivity for superoxide, immunology effects and stability\textsuperscript{37}.

It is reported the observation that the Mn(II) based SOD mimics inhibits superoxide mediated injury to human aortic endothelial cells\textsuperscript{70}. The superoxide is a product of activated polymorphonuclear leukocytes such as neutrophils, and has been proposed to be a mediator of inflammation\textsuperscript{71, 72}. 
2.6.7 Iron

The total content of iron in an adult body is 3 - 5 g. About 70% of this occurs in erythrocytes of blood as a constituent of hemoglobin. At least 5% of body iron is present in myoglobin of muscle. Heme is the most prominent iron containing substance. It is a constituent of several proteins/enzymes (hemoproteins) - hemoglobin, myoglobin, cytochromes, xanthine oxidase, catalase, tryptophan pyrrolase and peroxidase. Certain other proteins contain non-heme iron, e.g., transferrin, ferritin and hemosiderin. The iron requirement depends on age and gender of individuals, it is about 1-2.8 mg/day. All plants, animals and bacteria use iron, except for lactobacillus that appears to maintain high concentration of manganese instead of iron. The process and reactions in which iron participates are crucial to the survival of terrestrial organisms, and include ribonucleotide reduction (DNA synthesis), energy production (respiration), energy conservation (photosynthesis), nitrogen reduction, oxygen transport (respiration and muscle contraction) and oxygenation (e.g., steroid synthesis solubilisation and detoxification of aromatic compounds). Hemoglobin and myoglobin perform their major physiological role of reversible oxygen binding with iron in the iron(II) oxidation state, and many other hemoproteins function in this state, at least part of the time. The iron(II) hemoproteins, in several respects are thoroughly studied. Iron is stored mainly in ferritins, a family of proteins composed of protein coat and iron ore of hydrous ferric oxide with various amounts of phosphate. Ferritin is found in animals, plants and even in bacteria. Transferrin is responsible for the transportation of iron in biological system. The structure of mammalian transferrin has been deduced. The iron deficiency in human body is anemia. Hemosiderosis is due to excessive iron in the body. This is occurred as a result of excessive deposit of iron in ferritin and hemosiderin. Hemochromatosis is a rare disease, in which iron is directly deposited in the tissues (liver, spleen, pancreas and skin). The bleomycin (Blm) is a natural product, and is used in the treatment of some human cancer. The Blm is converted into FeBlm, to inhibit cell proliferation and degrade cellular DNA.
2.6.8 Cobalt

The total cobalt content of the body is 1 - 2 mg\(^{31}\). Cobalt has only one important biochemical role, which is in Vitamin-B\(_{12}\)\(^{29}\). Cobalt content of vitamin-B\(_{12}\) is about 4% by weight. This vitamin is a co-factor of a number of enzymes, which catalyze a number of biological reactions. Hence, cobalt has been assigned the status of an essential element. The Vitamin-B\(_{12}\) is a cynocomplex; but a methyl or methylene group replaces CN in native enzymes. Vitamin B\(_{12}\) deficiency causes severe disease of pernicious anemia in humans\(^{32}\). Many parallels exist between the chemistry of Fe\(^{II}\) and Co\(^{II}\) porphyrinato systems. Dioxygen binds to many Co\(^{II}\) complexes to give mononuclear 1:1 Co:O\(_2\) complexes and 2:1 Co:O\(_2\) complexes\(^{80,81}\). It was found that cobalt corrinss, such as vitamin B\(_{12}\), also formed 1:1 dioxygen adducts\(^{82}\), although this chemistry is not known to be utilized by living systems\(^{83}\). The hemoglobin and myoglobin may be reconstituted from the cobaltheme with preservation not only of dioxygen-binding capabilities but also of cooperatively\(^{84}\). The synthetic 1:1 Co:O\(_2\) complexes have proved to be very useful in increasing our understanding of factors that determine oxygen affinity for cobalt systems and by extrapolation of iron systems.

2.6.9 Nickel

Nickel is an activator of a number of enzymes, e.g., alkaline phosphate and oxataacetate decarboxylase, which can also be activated by other divalent metal ions. Nickel also enhances insulin activity\(^{31}\). The essential role of nickel has been established by inducing deficiency symptoms in feeding experiments with chickens and rat. The symptoms include change in liver mitochondria. The daily intake in normal food amounts to 150 - 170 µg. Nickel is a component of hydrolase (urease), of hydrogenase, of CO hydrogenase, and S-methyl COM reductase, which catalyses the terminal step in methane production by methanogenic bacteria\(^{32}\). All the nickel proteins known today are from plants or bacteria\(^{85,86}\). The function of nickel in the activation of gene for hydrogenase enzyme has been established\(^{87}\).
2.6.10 Copper

The body contains about 100 mg of copper distributed in different organs\[^{30}\]. Copper is a component of a number of oxidoreductase enzymes (cytochrome oxidase, superoxide dismutase, triosinase and uricaseaminooxidase)\[^{31}\]. In blood plasma, it is bound to ceruloplasmin, which catalyzes the oxidation of the Fe\(^{2+}\) to Fe\(^{3+}\). The reaction is of great significance since it is only the Fe\(^{3+}\) form in blood which is transported by the transferrin protein to the iron pool in the liver. The daily copper requirement is 1 - 2 mg, and it is supplied in normal diet. The use of stored iron is reduced by copper deficiency, which suggests that iron metabolism may depend on copper proteins, such as serumproteinceruloplasmin, which can function as ferroxidase, and the cellular protein ascorbic acid oxidase, which also is a ferrireductase\[^{32}\]. Studies have evolved to give evidence to suggest that the normal taste acuity\[^{88}\] and normal development of bone\[^{89}\] and collagen\[^{90,91}\] are dependent on copper. Copper atoms are integral part of ceruloplasmin structure, and remain attached to the protein during its entire life span in circulation\[^{92}\]. There is no exchange of copper with injected inorganic radioactive copper in vivo. Consequently, hypothesis of ceruloplasmin’s physiological function, which postulates reversible ionization of copper from the protein are improbable.

The oxidase activity of ceruloplasmins is a function of the reversible reduction of cupric ions by substrate and oxygen\[^{93}\]. The ceruloplasmins, like many plasma proteins, are synthesized in liver\[^{94}\], and the rate appears to be under hormonal control\[^{95}\]. Ceruloplasmin is also found in spinal fluid, lymph, joint fluid, lacrimal, nasal and gastrointestinal secretions\[^{96,97}\].

Severe deficiency of copper causes demineralization of bones, demyelination of neural tissues, anemia, fragility of arteries, myocardial fibrosis, hypopigmentation of skin and graying of hair. Wilson disease\[^{98}\] results from a genetically inherited metabolic defect, in which copper can no longer be tolerated
at normal levels. The clinical manifestations are liver disease, neurological damage and browner green rings in the cornea of eyes. The redox activity of copper complexes has been utilized to design new drugs for the purpose of inhibiting and killing tumor cells. Mono- and bis-thiosemicarbazones were among the first compounds that were deliberately constructed as metal binding ligands for this purpose. These are showing strong antitumor effect when administered to host, depending up on the presence of copper in the host.

2.6.11 Zinc

The total content of zinc in an adult body is about 2 g. Prostrate gland is very rich in zinc (100µg/g). Zinc is mainly an intracellular element. Zinc is relatively abundant in biological materials. It is an essential component of several enzymes, e.g., carbonic anhydrase, alcohol dehydrogenase, alkaline phosphates, carboxypeptidase and superoxide dismutase. The storage and secretion of insulin from the β-cells of pancreas requires zinc. Zinc is necessary to maintain the normal levels of vitamin A in serum. Gusten, a zinc containing protein of saliva is important for taste sensation. Zinc is essential for the proper reproduction. The major location of zinc in the body is metallothionein. Like the ferritin, metallothionein is a family of proteins, wide spread in nature and regulated by metals they bind. Metallothioneins especially in higher animals are small proteins. Zinc is a common element in nucleic acid-polymersases and transcription factors, where its role is considered to be structural rather than catalytic. A group of nucleic acid binding proteins, with a repeated sequence containing the amino acids, cysteine and histidine, which are shown to bind as many as eleven zinc atoms necessary for protein function, have been investigated.

Zinc plays a structural role forming the peptide in to multiple domains or “zinc fingers” by means of coordination to cysteine and histidine. A class of genetic factors containing “zinc fingers” are zinc proteins, in which the metal has an essentially structural role. Zinc in the “zinc finger” regulatory protein is playing an important role in functioning of nucleic acid. Zinc has a specific role in bioinorganic processes because of the peculiar properties of coordination.
compounds of Zn(II) ions. Zinc can easily be four, five or six coordinate with out a marked preference of six coordination. Secondly, the coordinated water molecule in enzyme is kinetically labile. A new role of zinc has been developing for the treatment of human immuno deficiency disease. The human immuno deficiency disease virus type 1 (HIV-1) is the etiological agent of acquired immune deficiency syndrome (AIDS). A relatively recent target for drug design has been the “zinc fingers” of the nucleocapsid protein\textsuperscript{107}. A principal approach has been to design chelating agents such as dithiobis benzamides (DIBAs), which chemically modifies the zinc finger cysteine residues resulting in zinc ejection from the fingers with resultant inhibition of HIV replication\textsuperscript{37}.

2.6.12 Tin

Tin is an ultratrace element encountered in human tissues\textsuperscript{34}. The essentiality of the bulk requirement element is easy to determine, but it is very challenging to identity elements that organisms need in tiny quantities - the ultratrace elements. Because, we need so little of them, it is almost impossible to eliminate them from the normal diet to examine the effects of any deficiency. Thus, the biological function of tin is also to be studied further. Although growth promoting effect of tin has been detected in rats, it is disputed\textsuperscript{31}. The organic tin compounds are toxic.

2.7 Thermal analysis - a brief overview

Thermal analysis (TA) is a general term covering a group of related techniques, where by the dependence of the parameters of any physical property of a substance on temperature is measured. The history of the development of TA methods from earliest times is considered in papers by Meckenzie\textsuperscript{108}, which include an account of thermometry developed in the sixteenth century. Thermal analysis methods are now used in a very large range of scientific investigations.

Since TA methods had been developed by many workers, it was necessary to agree on a common terminology, and the International Confederation for Thermal Analysis and Calorimetry (ICTAC) has made recommendations on the
nomenclature and calibration methods, which are to be used\textsuperscript{109 - 112}. Thus, thermal analysis has been defined as "a group of techniques, in which a property of a sample is monitored against time or temperature programmed in a specified atmosphere. The programme may involve heating or cooling at a fixed rate of temperature change, or holding the temperature constant, or any sequence of these. Based on the physical property measured, the thermal analysis techniques are broadly classified and these are tabulated in Table 2.1\textsuperscript{113}.

Surveys of various thermal analysis techniques used and their applications to numerous areas of research have been published by Wendlandt, Liptay and Dunn\textsuperscript{114 - 116}. The most widely used techniques are thermogravimetry (TG), derivative thermogravimetry (DTG), differential thermal analysis (DTA), differential scanning calorimetry (DSC) and thermomechanical analysis (TMA). Thermal analysis techniques are extensively used in the studies of inorganic materials, polymers, metals, alloys and organic substances.

### 2.7.1 Basis of thermal analysis

Every substance is characterised by its free energy, $G$ as given by the expression

$$G = H - TS$$

where $H$ is the enthalpy, $T$ is the temperature in Kelvin and $S$ is the entropy. At a given temperature, every system has a tendency to attain a state in which the free energy is at minimum. The formation of more stable crystalline structure (solid state phase change) or another state with lower free energy may take place on gradually heating the sample, \textit{via} intermediate steps\textsuperscript{117}. All these transformations are characterized by the temperature at which it occurs and by a change in the heat content as manifested by an increase or decrease in the temperature depending on whether the reaction is exothermic or endothermic, respectively. Sometimes, the change in heat content is accompanied by a change in mass, and the observation of such a change is the basis of TG. When the substance is heated or cooled, and is reversible or irreversible, change in its dimension takes place, which is the basis of dilatometry.
In the present investigation TG, DTG and DTA techniques are used to follow the thermal decomposition studies.

2.8 Thermogravimetry

The origin of thermogravimetry (TG) has been fully documented by Duval118, Keattch and Dollimore119, and Wendlandt120. The most significant contribution was made by Honda in 1915121, who used a lever arm balance fitted with an electrical furnace to investigate manganese oxy salts. Simple experimental apparatus has been described, which uses modified manual analytical balance and controlled electric furnace122. The Chevanard thermobalance was the first to record mass changes automatically using a photographic plate. This was extensively used from 1936 by Duval and others123. The development of electronic microbalance allowed smaller samples and furnaces to be used, and work to be carried out in controlled atmosphere and in vacuum124. Thermogravimetry is a technique in which the mass of the sample is monitored against time or temperature while the temperature of the sample in a specified atmosphere is programmed. In order to enhance the steps in the thermogravimetric curve, the derivative thermogravimetric (DTG) trace is frequently drawn.

The applications of TG and the factors affecting TG were discussed by Wendlandt125. The modern aspect of TG began in the late 1950s with the work of Duval, who used thermobalance to describe a method in analytical chemistry called automated gravimetric analysis117, 126 - 129. At present, the most widely used thermal analysis technique to study the solid state thermal decomposition reaction is TG130. The data obtained from TG are more quantitative than those obtained from DTA or DSC, because mass measurement (in TG) has an order of magnitude of higher accuracy and precision compared to the measurement of T (in DTA) or dH/dt (in DSC). A statistical analysis to demonstrate the variance of the kinetic parameters obtained from TG, DTA and DSC have better precision than those obtained from the other two methods131, 132. However, TG is a more limited
technique compared to DTA or DSC in the sense that TG study is applicable to a limited number of reactions, which involve mass changes.

### 2.8.1 Factors-affecting thermogravimetric experiments

Being an instrumental technique, a large number of factors affect the nature, precision and accuracy of thermogravimetric experimental results. Thermogravimetry probably has a number of variables because of the dynamic nature of the temperature change of sample. Duval discussed in detail the precautions involved in using a thermobalance as well as many other variables involved in thermogravimetry\(^\text{118,126}\). The factors affecting thermogravimetry have been classified as (i) instrumental factors consisting of furnace heating rate, atmosphere, geometry of sample holder and furnace, recording or chart speed, sensitivity of recording mechanism and composition of sample container, and (ii) sample characteristics such as sample mass, particle size, sample packing, thermal conductivity, nature of sample, heat of reaction and solubility of evolved gas. Wendlandt discussed the effect of these parameters on the shape of thermogravimetric curves, and hence, the reliability of experimental results\(^\text{125}\). A number of studies have been carried out to evaluate the effect of procedural factors such as heating rate and sample mass on kinetic parameters and mechanism of various types of reactions\(^\text{133 - 142}\). Some empirical relations connecting these factors with the kinetic parameters have also been derived\(^\text{143 - 147}\).

### 2.9 Derivative thermogravimetry

Dekeyser\(^\text{148,149}\) first suggested derivative thermogravimetric (DTG) technique in 1953 followed by Erde\(^\text{150}\) and Waters\(^\text{151}\). In this technique, the first derivative of mass change with respect to time is recorded as a function of time or temperature. In the DTG curve the first derivative, \(\frac{dm}{dt}\) is plotted on the ordinate with mass loss downwards and t or T on the abscissa increasing from left to right\(^\text{118}\). The maximum of the DTG curve represents the inflection point, where the rate of mass loss is maximum. The area under the DTG curve is directly proportional to the mass change, and the height of the DTG curve gives the rate of mass change at that temperature. The DTG curve allows the ready determination
of the temperature at which the mass change is maximum (T_s) and the initial temperature (T_i) at which cumulative mass change begins and the final temperature (T_f) at which the cumulative mass change ceases for that particular stage of change. The DTG curve is of assistance if there are overlapping reactions. Even though the position of peak may not be indicative of any characteristic point in the mechanism of the reaction, only where mass loss is fastest. However the peak may be used as a “finger print” to identify the presence of a substance in a mixture e.g. a particular mineral in a rock or oil sample.\(^{152}\)

### 2.10 Differential thermal analysis

Differential thermal analysis (DTA) is a thermal technique, in which the temperature of the sample compared with the temperature of a thermally inert material is recorded as a function of temperature of the inert material or furnace temperature as the sample and the reference material are heated or cooled at a uniform rate. It is a differential method, in which the difference in temperature, \( T_{\text{sample}} - T_{\text{reference}} (\Delta T) \) is recorded as a function of temperature. \( \alpha \)-Alumina is used as the reference material because it does not undergo decomposition or any thermal change up to \( \sim 1950^\circ\text{C} \).

The history of DTA has been described by Mackenzie\(^ {108}\). Le' Chatelier (1887) seems to be the first person, who has recorded temperature as a function of time in heating curves\(^ {153, 154}\). The method of cooling curve was introduced by Burgess in 1908\(^ {155}\). Complete DTA, \( i.e. \), time, temperature difference and temperature measurements, was first determined by an English metallurgist, Roberts Austin\(^ {156}\). Saladin developed a photographic record of \( \Delta T \) versus \( T \) directly\(^ {157}\), and Kurnakov used a versatile photographic recorder based on a rotating drum\(^ {158}\). A critical study of DTA method for the identification of clay minerals was made by Norton\(^ {159}\). An important development in DTA instrumentation was brought about by Stone, who used it in controlled atmosphere such as water or carbon dioxide\(^ {160}\).
Analytical applications of DTA have been reviewed by Garn\textsuperscript{161}. David has used DTA for the measurement of specific heat and heat of fusion\textsuperscript{162}. Borchardt and Daniels developed the necessary theory for the application of DTA to the study of reaction kinetics\textsuperscript{163}. Kissinger in the same year independently derived a method to evaluate activation energy from DTA measurements\textsuperscript{164}. The DTA is now a days extensively used for the study of heterogeneous reaction kinetics.

2.11 Differential scanning calorimetry

The term, DSC was apparently first used by Watson to describe the instrumental technique developed by Perkin-Elmer Corporation in 1963\textsuperscript{165}. The DSC is a technique of the energy necessary to establish zero temperature between the substance and a reference material against either time or temperature as the two specimens are subjected to identical temperature regimes in an environment heated or cooled at controlled rate. The curve obtained is a recording of heat flow, $dH/dt$ as a function of temperature. A peak in the upward direction indicates an exothermic peak, while the endothermic peak is recorded in the downward direction. The kinetics and mechanism of solid state thermal decomposition reactions can be studied using DSC\textsuperscript{166,167}.

In all appearances, a DSC curve looks very similar to that of a DTA curve except for the ordinate axis unit. The DSC measurements are considered to be more quantitative than DTA, and therefore, the former is more popular whenever small energy changes are measured.

2.12 Simultaneous TG/DTA measurements

The dynamic nature of thermal methods affects the results, we obtain. The results will depend up on the nature of the sample, crucible or sample holder, rate of heating, atmosphere and mass of the sample. It would, therefore, be an advantage to use the same sample, heating rate and other conditions and to sense the properties simultaneously. The coupled thermal techniques such as simultaneous TG/DTA are also referred to as 'hyphenated techniques'. The early work by Paulik \textit{et al} used the derivatograph to measure simultaneously the TG,
DTG and DTA data\textsuperscript{168}. Later, new sophisticated instruments were designed for this purpose. The techniques of simultaneous measurement save both the time and sample. Most important is that it gives results for two or more techniques under precisely the same experimental conditions.

It might be possible to combine many analytical techniques, both conventional and thermal, together in a single thermal analysis system. One example of such a system was used in space exploration, and produced data on the nature of the surface of Mars\textsuperscript{169}. Uden \textit{et al} have combined thermal analyzers, pyrolysis furnaces, gas chromatography, vapour phase IR, mass spectrometry and elemental analysis\textsuperscript{170}.

The field is dominated by the advent of microthermal analysis\textsuperscript{171}. This is a relatively new technique that involves an analysis region of a few micrometers, which is investigated using a combination of atomic force microscopy and differential thermal analysis. The technique of temperature modulated scanning calorimetry is continually receiving a great deal of attention. Ozawa reviews the applicability and limitation of this technique\textsuperscript{172}. He has used computer simulation to elucidate the response of the equipment to abrupt changes in heat capacity\textsuperscript{173}. Computer simulations dealing with the melting kinetics of polymer crystals under a regime of modulated temperature are also reported\textsuperscript{174}. Simon and McKenna used the tool called ‘Narayanaswamy-Moynihan equation’ to determine the effects of structural recovery and thermal lag in modulated DSC measurements\textsuperscript{175}. A comprehensive theoretical paper on phase transitions observed with the use of temperature modulated differential scanning calorimetry (TMDSC) is provided by Hohne\textsuperscript{176}. Wunderlich \textit{et al} have dealt with the subject of cell asymmetry correction for TMDSC\textsuperscript{177}, and also looked at the use of the higher harmonics of Fourier transform\textsuperscript{178}.

The uses of DTA and DSC at high pressures have been described in many earlier publications, and are included in many “primers” on thermal analysis. Schmidt \textit{et al} used this technique to follow transformation of liquid crystal and a triglyceride up to 300 MPa\textsuperscript{179}. Pulse thermal analysis (PTA) is based on injection
of the gaseous reactants into an inert carrier gas stream followed by monitoring the changes in mass, enthalpy and gas composition resulting from an incremental change in the gas-solid reaction. It is illustrated by Maciejewski and Baiker with respect to various reactions. Extensive reviews on the evolved gas analysis using mass spectrometry and infrared spectrometry are available.

2.13 Kinetics of solid state thermal decomposition reactions

Study of solid state reaction has three aspects, viz., phenomenological, thermodynamic and kinetic aspects. The phenomenological study is concerned with the quantitative and semiquantitative observations of the phenomena occurring during the reaction. The thermodynamic approach is static in its outlook. It relates to the initial, final and equilibrium states of the systems and to the driving force behind the transformation. The kinetic study deals with the rate of transformation of the reactants into products and the mechanism of transformation.

The nature of solid state reactions is quite complex. In general, the reaction proceeds stepwise, and it involves a number intermediate reactions in series, which result in the formation and decomposition of several solid or liquid phases. The different solid state reactions are

i. Reaction of a single solid

\[ A_{(s)} \rightarrow B_{(s)} + C_{(g)} \]

ii. Reaction between two solid phases, where gas is also evolved

\[ A_{(s)} + B_{(s)} \rightarrow AB_{(s)} + C_{(g)} \]

iii. Reaction which is confined only to solid phases

\[ A_{(s)} + B_{(s)} \rightarrow C_{(s)} + D_{(s)} \]

iv. Reaction involving liquid phase at some stages of the reaction

\[ A_{(s)} \rightarrow B_{(s)} + C_{(l)} \]
v. Reaction between a solid and a gas

$$A(s) + B(g) \rightarrow C(s)$$

The above reactions may occur either successively or simultaneously. Thermogravimetry is generally concerned with only a single substance. Hence, only reactions of the types (i) and (iv) are applicable.

The general approach in kinetic analysis is to obtain an equation for the rate of reaction. In the case of solid state decomposition reaction of the type

$$A_{\text{solid}} \rightarrow B_{\text{solid}} + C_{\text{gas}}$$

the rate of decomposition can be considered as the product of two functions of temperature and conversion. That is, the rate is expressed as

$$\frac{d\alpha}{dt} = k(T)f(\alpha) \quad \text{................................. (1)}$$

where $\alpha$ is the fraction decomposed in time $t$, $k(T)$ is the temperature dependent and $f(\alpha)$ depends on the mechanism of the process. It has been established that for most of the reactions, the temperature dependence is found to be the Arrhenius type so that the term, $k(T)$ can be considered as the rate constant, $k$, i.e.,

$$k = A e^{-\frac{E}{RT}} \quad \text{................................. (2)}$$

where $A$ is the pre-exponential factor, $E$ is the activation energy, $R$ is the gas constant and $T$ the temperature in Kelvin. Substituting equation (2) in equation (1), we get

$$\frac{d\alpha}{dt} = Ae^{-\frac{E}{RT}} f(\alpha) \quad \text{................................. (3)}$$

There are two basic approaches in solving this equation, i.e., mechanism non-invoking method and mechanism invoking method.
2.13.1 Mechanism non-invoking method

The mechanism non-invoking method is a simple extension of homogenous kinetics, where the conversion function, \( f(\alpha) \) is assumed to be of the form

\[
f(\alpha) = \alpha^m (1 - \alpha)^n \]

where 'm' and 'n' are called homogeneity factors. This equation has been derived from theoretical models or from experimental data.

When 'm' is assumed to be zero, the homogeneity factor 'n' can be identified with the reaction order, 'n'. It is unjust to use the term 'order of reaction' in the same sense as used in homogenous kinetics. So, 'n' has been described as 'order parameter' implying to have only empirical significance.

Based on the above, the rate equation can be written as

\[
\frac{d\alpha}{dt} = A e^{-\frac{E}{RT}} (1 - \alpha)^n
\]

The three basic parameters \( \text{viz.} \), order parameter (n), energy of activation (E), and pre-exponential factor (A) for a given change have to found out, for the evaluation of kinetic factors.

Two approaches are normally used for this purpose, \( \text{viz.} \), isothermal and non-isothermal methods.

**Isothermal method**

Isothermal method is the conventional method for the evaluation of kinetic parameters. It is based on the observation of the reaction at constant temperature. Isothermal method consists of carrying out several runs at different constant temperatures, the mass change being recorded at each of these temperatures as a function of time.
In isothermal kinetics, the kinetic parameters are evaluated based on the rate equation,

\[
\frac{da}{dt} = k(1 - a)^n
\] ................................. (6)

For the correct value of ‘n’ a plot of \( \frac{da}{dt} \) vs \((1-a)^n\) will give a straight line with slope = \( k \). However, the accuracy of determination of the tangent, \( \frac{da}{dt} \) is basically poor, and hence, the integral approach is normally preferred. Rearranging equation (6) and integrating we get,

\[
\frac{1-(1-a)^{1-n}}{1-n} = kt
\] .............................. .. (7)

This equation is applicable to all values of ‘n’, except \( n = 1 \). When \( n = 1 \), the equation becomes,

\[-\ln(1-a) = kt \] ................................. (8)

The LHSs of equations (7) and (8) are called \( g(a) \), for convenience. Thus, a plot of \( g(a) \) versus ‘t’ gives a straight line with slope = \( k \). The plots can be made for various values of ‘n’, and the order parameter is chosen as the one, which gives the best straight line plot (with maximum correlation coefficient). The rate constant, \( k \) evaluated at different temperatures and from \( \ln(k) \) versus 1/T plots, ‘E’ and ‘A’ can be calculated.

A prior knowledge of the correct form of \( g(a) \), i.e., the correct value of ‘n’ is required for the evaluation of kinetic parameters by this method, unless one resorts to the iteration method of trying various values of ‘n’. It has been attempted to circumvent this problem by a ‘\( g(a) \)-free’ approach. From equations (2) and (7) we obtain,

\[
g(a) = kt = Ae^{-\frac{E}{RT}} \] t ................................. (9)

or
Materials and methods

\[ \ln(t) = \ln g(a) - \ln A + \frac{E}{RT} \]

(10)

Since \( \ln g(\alpha) \) is very small in comparison to \( \ln A \), E and A can be obtained from plots of \( \ln t \) versus \( 1/T \) and usually \( t_{1/2} \), i.e., the time taken for \( \alpha = 0.5 \) is used for this purpose. The dependence of kinetic parameters on the specific value chosen has been evaluated, which shows a pronounced dependence of E and A on the value chosen\(^{141}\). Vyazovkin denied the concept of constant activation energy, and suggests as alternative, the concept of 'variable activation energy', which is an unpredictable function of temperature and/or extent of reaction\(^{183, 184}\). L'vov developed a new concept of third law method for the thermal analysis of solids to get better results\(^{185}\).

One drawback of isothermal method is that it is often difficult to follow solid state reaction isothermally due to the temperature lag between the sample and furnace.

**Non-isothermal or dynamic method**

In this method the mass change is recorded as a function of temperature, the substance being heated at constant (linear) heating rate. That is, \( T = T_0 + \phi \), where \( T_0 \) and \( T \) represent the temperature at time \( t = 0 \) and \( t = t \) and, \( \phi = dT/dt \) is the heating rate. Non-isothermal method has more advantages than the conventional isothermal method to determine the kinetic parameters\(^{125}\). The non-isothermal method has the following advantages.

a. Considerably fewer data are required.

b. The kinetics can be calculated over an entire temperature range in a continuous manner.

c. Only a single sample is required

d. The results are obtained from a single measurement unlike the isothermal method, in which several measurements are required.
There are two approaches for this evaluation of kinetic parameters of thermal decomposition reactions under non-isothermal conditions.\(^{130}\)

a) A general kinetic study, which is a simple extension of homogeneous kinetics to solid state (usually heterogeneous) study.

b) A mechanism based study, which gives the physicochemical description of the process proposed on the basis of a certain model.

For a linear heating rate

\[
\frac{dT}{dt} = \phi.
\]

Combining equation (5) and the above, we get

\[
\frac{d\alpha}{dT} = \frac{A}{\phi} e^{-\frac{E}{RT}} (1-\alpha)^n \quad \text{......................... (11)}
\]

where ‘\(\alpha\)’ is the fraction of the sample decomposed for the solid state reaction of the type

\[\text{A}_{\text{solid}} \rightarrow \text{B}_{\text{solid}} + \text{C}_{\text{gas}}\]

and \(\alpha\) is given by the relation

\[
\alpha = \frac{w_t}{w_\alpha} = \frac{(m_0 - m_t)}{(m_0 - m_\alpha)}
\]

where \(w_t\) = mass loss at time, \(t\)

\(w_\alpha\) = maximum mass loss

\(m_0\) = initial mass of the sample

\(m_t\) = mass at time \(t\) and

\(m_\alpha\) = mass at the end of the reaction
Equation (11) is the fundamental equation used in non-isotherm thermogravimetry employing a linear heating rate.

Several attempts have been made by various scientists to derive convenient workable equations from equation (11), which could form the basis for the evaluation of kinetic parameters, A and E. The following three different approaches have been made in this context.

a. Differential method

b. Approximation method

c. Integral method

Before proceeding, some common terms may be defined, as given below.

The term, \( w_r \) may be defined as \( w(a) - w(t) \); \( w_r \) would represent the mass loss that has yet to occur between time \( t \) and \( t_f \). It can be seen that

\[
\alpha = \frac{(w_t - w_r)}{(w_a)}
\]

Another term, \( C \) may be defined as \( C = 1 - \alpha \). Then, it follows that

\[
C = \frac{(w_a - w_t)}{(w_a)} = \frac{w_t}{w_a}
\]

a. Differential method

The most widely used differential method to get the kinetic parameters is the method introduced by Freeman and Carroll\(^{186}\). This equation has the form

\[
\frac{\Delta \log (dw/dt)}{\Delta \log (w_r)} = \frac{E}{2.303 R} \frac{\Delta (1/T)}{\Delta \log (w_r)} \tag{12}
\]
In this equation, \( \frac{dw}{dt} \) represents the time slope, which is not directly obtained from the experimented data. This equation can be transformed into a more convenient form to get the temperature slope as follows.

Since the rate of heating is given as \( \phi = \frac{dT}{dt} \),

\[
\frac{dw}{dt} = \frac{dw}{dT} \times \frac{dT}{dt} = \frac{dw}{dT} \phi
\]

\[
\Delta \log\left(\frac{dw}{dt}\right) = \left[\log\left(\frac{dw}{dT}\right)\right] - \left[\log\left(\frac{dw}{dT}\right)\right] \\
= \left[\log\left(\frac{dw}{dT}\right)\right] + \log\phi - \left[\log\left(\frac{dw}{dT}\right)\right] - \log\phi \\
= \Delta \left[\log\left(\frac{dw}{dT}\right)\right]
\]

Hence, the original Freeman-Carroll equation can be alerted into equation

\[
\frac{\Delta \log\left(\frac{dw}{dt}\right)}{\Delta \log\left(w,\right)} = -\frac{E}{\Delta (1/T)} = \frac{\Delta (1/T)}{\Delta \log\left(w,\right)} + n 
\]

where \( \frac{dw}{dt} \) is the slope of the mass loss with respect to temperature, \( T \). Plotting the LHS of equation (13) versus \( \frac{\Delta (1/T)}{\Delta \log\left(w,\right)} \), a straight line would be obtained. The intercept would give the value of ‘\( n \)’, and the value of \( E \) can be obtained from the slope.

The Freeman-Carroll equation can be applied to a number of dehydration reactions. The main disadvantage of this method is that the determination of the slope, \( \frac{dw}{dt} \) is a tedious process requiring either drawing tangents or applications of the method of numerical differentiation. It may also be noted that some doubts have been expressed about the reliability of the values of ‘\( n \)’ obtained by the differential method.

b. Approximation method

The approximation method employs an approximation related, usually to a particular experimentally determined value such as inflection point of TG curve. Van-Krevelen developed the first equation in this series\(^{187}\). The Horowitz-
Metzger method may be used to illustrate the approximation method\textsuperscript{188}. The following relationships were used.

\[
\log \left[ \frac{1 - C^{(i-n)}}{1 - n} \right] = \frac{E\theta}{2.303RT_s} + \log \frac{\text{ART}_s^2}{E\phi} - \frac{E}{2.303RT_s}
\]

\[
\log \left[ \frac{1 - C^{(i-n)}}{1 - n} \right] = \frac{E\theta}{2.303RT_s} + \text{constant, when } n \neq 1 \tag{14}
\]

\[
\log [\ln C^{-1}] = \frac{E\theta}{2.303RT_s} + \log \frac{\text{ART}_s^2}{E\phi} - \frac{E}{2.303RT_s}
\]

\[
\log [\ln C^{-1}] = \frac{E\theta}{2.303RT_s} + \text{constant, when } n = 1 \tag{15}
\]

where \(T_s\) is the temperature of maximum decomposition and \(\theta = T - T_s\). The value of \(T_s\) may be obtained from the derivative thermogravimetric (DTG) curve, where it will appear at the peak temperature.

Unlike the Freeman-Carroll method, prior determination of the order parameter, ‘n’ is necessary here. This may be done by making use of the following relation put forward by Horowitz and Metzger

\[
C_s = n^{1/(1-n)} \tag{16}
\]

The approximation method is generally considered to be the least accurate of the methods, but mathematically it is simpler than any other method.

c. \textit{Integral method}

Integral method is regarded as the most accurate of the various methods for the evaluation of kinetic parameters from the TG data\textsuperscript{189, 190}. For this we can recall the equation (11)
\[
\frac{d\alpha}{dT} = \frac{A}{\phi} e^{\frac{-E}{RT}} (1 - \alpha)^n
\]

Rearranging the above equation, we get

\[
\frac{d\alpha}{(1 - \alpha)^n} = \frac{A}{\phi} e^{\frac{E}{RT}} dT \quad \text{................................. (17)}
\]

On integration of the above equation, we have

\[
\int_0^\alpha \frac{d\alpha}{(1 - \alpha)^n} = \frac{A}{\phi} \int_0^T e^{\frac{E}{RT}} dT \quad \text{................................. (18)}
\]

The LHS of equation (18) can readily be integrated. For convenience, this expression will be denoted by \( g(\alpha) \)

when \( n \neq 1 \)

\[
g(\alpha) = \left[ \frac{1 - C^{(l-n)}}{1-n} \right]
\]

and when \( n = 1 \)

\[
g(\alpha) = \ln C^{-1}
\]

The temperature integral of RHS of equation (18) cannot be integrated easily. Several attempts have been made to evaluate the temperature integral. The approach of Coats and Redfern is one of the most widely accepted integral methods\(^{192}\).

Coats and Redfern made use of Rein Ville function in evaluating the temperature integral\(^{191}\), and obtained the relation,

\[
\frac{A}{\phi} \int_0^T e^{\frac{-E}{RT}} dT = \frac{AR}{\phi E} \left( 1 - \frac{2RT}{E} \right) T^2 e^{\frac{E}{RT}} \quad \text{................................. (19)}
\]
Combining equations (18) and (19) and using the notation \( g(\alpha) \), we get

\[
\log \frac{g(\alpha)}{T^2} = \log \left[ \frac{A}{\phi E} \left( 1 - \frac{2RT}{E} \right) \right] - \frac{E}{2.303RT} \quad (20)
\]

Equation (20) is the Coats Redfern equation. This equation may be given in the following forms,

\[
\log \left[ \frac{1 - C^{i-n}}{(1-n)T^2} \right] = \log \left[ \frac{A}{\phi E} \left( 1 - \frac{2RT}{E} \right) \right] - \frac{E}{2.303RT}, \quad \text{when } n \neq 1
\]

and

\[
\log \left[ \frac{C^{-1}}{T^2} \right] = \log \left[ \frac{A}{\phi E} \left( 1 - \frac{2RT}{E} \right) \right] - \frac{E}{2.303RT}, \quad \text{when } n = 1
\]

Coats and Redfern have further shown that for the usual values of temperature range, over which reaction generally occurs, the term \( \log \left[ \frac{A}{\phi E} \left( 1 - \frac{2RT}{E} \right) \right] \) is practically constant; and the term \( (2RT/E) \) can be neglected, since the value is very small\(^{192} \). Therefore, equation (20) is reduced to

\[
\log \frac{g(\alpha)}{T^2} = \log \left[ \frac{A}{\phi E} \right] - \frac{E}{2.303RT} \quad (21)
\]

where \( g(\alpha) = \left[ \frac{1 - C^{i-n}}{(1-n)} \right], \quad \text{when } n \neq 1 \)

and \( g(\alpha) = \ln C^{-1}, \quad \text{when } n = 1 \)

A plot of \( \log g(\alpha)/T^2 \) verses \( 1/T \) would, therefore, give a straight line, whose slope is equal to \( E/2.303R \), and the intercept is equal to \( \log A/\phi E \). From the slope and the intercept, \( E \) and \( A \) can be calculated, respectively.
The entropy of activation, $\Delta S$, is calculated from the equation given below.

$$A = \frac{kT_s \Delta S}{h}$$

where $k$ is the Boltzmann constant, $T_s$ is the temperature at which the maximum decomposition takes place, which can be directly read off from the DTG curve. The disadvantages of integral method are the following.

a) Prior determination of ‘n’ is required.

b) Temperature integral is often evaluated by mathematical approximation.

c) The kinetic parameters obtained are found to be rather insensitive to changes in ‘n’.

2.13.2 Mechanism invoking method

The elucidation of the mechanism of the reaction under study is a major concern of chemical kinetics. The elucidation of the reaction mechanism for solid state thermal decomposition reactions is more complicated than in the case of homogeneous reactions. The heterogeneous process can be broadly classified into there basic steps, viz.,

a) Nucleation and growth of nuclei

b) Diffusion (transport of matter)

c) Phase boundary reaction

The basic mechanism of thermal decomposition involves the formation and propagation of the ‘nuclei’, which is denoted by nucleation and ‘growth’. Nucleation has been shown to be a surface phenomenon associated essentially with surface defects. All the thermal decomposition reactions involve nucleation. Various rate equations based on the mechanisms have been put
forward for solid state thermal decomposition reactions. These equations incorporate the laws of diffusion, nucleus formation and growth of nuclei, and phase boundary movements in some form or other.

As has been stated that \( f(\alpha) = (1-\alpha)^n \), depending up on the mechanism involved in the decomposition reaction, ‘n’ will have different values. For example, \( n = 0 \) represents either a fusion process or a reaction involving a high degree of surface absorption. When \( n = 1/2 \) or \( n = 2/3 \), the mechanism is phase boundary reactions in two or three dimension, respectively. When \( n = 1 \), the rate is controlled by random nucleation. The \( g(\alpha) \) forms corresponding to various mechanisms have been derived for all these three processes assuming different physicogeometric models, and nine of them are listed in the Table 2.2 as proposed by Satava\(^{195}\).

Mamleev et al made extensive study on the modeling of non-isothermal kinetics in thermogravimetry\(^{196}\), in which 18 models were encountered as shown in the Table 2.3. A new algorithm is proposed for computing activation energy and rate constants by approximating on a set of TGA curves obtained over a wide temperature range and with arbitrary temperature-time relationship. Analysis with several heating rates gave quite reliable results. It is noteworthy that even if these models do not reflect a real physical degradation, they provide a good approximation for an activation energy.

For the purpose of calculating kinetic parameters, the non-isothermal method has the advantage of greater simplicity. The data collected for the TG measurements could be used without any additional work for the evaluation of kinetic parameters by employing the kinetic equations developed for the use of non-isothermal TG only, and hence, this procedure was followed in the present investigation of thermal decomposition studies of samples of glucose, fructose, sucrose, maltose and lactose impregnated with biologically active metals.
### Table 2.1 The important thermal analysis techniques

<table>
<thead>
<tr>
<th>Name of method</th>
<th>Symbol</th>
<th>Property measured</th>
</tr>
</thead>
<tbody>
<tr>
<td>Thermal analysis (Group name)</td>
<td>TA</td>
<td>Range of properties</td>
</tr>
<tr>
<td>Thermogravimetry</td>
<td>TG</td>
<td>Mass</td>
</tr>
<tr>
<td>Derivative thermogravimetry</td>
<td>DTG</td>
<td>First derivative of mass change</td>
</tr>
<tr>
<td>Differential thermal analysis</td>
<td>DTA</td>
<td>Differential temperature</td>
</tr>
<tr>
<td>Differential scanning calorimetry</td>
<td>DSC</td>
<td>Enthalpy</td>
</tr>
<tr>
<td>Thermomechanical analysis</td>
<td>TMA</td>
<td>Mechanical properties</td>
</tr>
<tr>
<td>Thermodilatometry</td>
<td>--</td>
<td>Dimensions</td>
</tr>
<tr>
<td>Evolved gas detection</td>
<td>EGD</td>
<td>Evolved gas detection — thermal conductivity</td>
</tr>
<tr>
<td>Evolved gas analysis</td>
<td>EGA</td>
<td>Identity and amount of gas evolved</td>
</tr>
<tr>
<td>Thermomagnetometry</td>
<td>TM</td>
<td>Magnetic properties</td>
</tr>
<tr>
<td>Emanation thermal analysis</td>
<td>ETA</td>
<td>Radio active gas</td>
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<tr>
<td>Thermosonimetry</td>
<td>TS</td>
<td>Acoustic properties</td>
</tr>
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<td>Thermooptometry</td>
<td>--</td>
<td>Optical properties</td>
</tr>
<tr>
<td>Thermoelectrometry</td>
<td>--</td>
<td>Electrical properties</td>
</tr>
<tr>
<td>Dielectric thermal analysis</td>
<td>DETA</td>
<td>Dielectric constant</td>
</tr>
<tr>
<td>Thermoluminescence</td>
<td>TL</td>
<td>Light emission</td>
</tr>
<tr>
<td>Variable temperature XRD</td>
<td>--</td>
<td>XRD patterns</td>
</tr>
<tr>
<td>Proton magnetic resonance thermal analysis</td>
<td>PMRTA</td>
<td>NMR determinations</td>
</tr>
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</table>
Table 2.2  The commonly used mechanistic equations for solid state reaction

<table>
<thead>
<tr>
<th>Function</th>
<th>Form of g((\alpha))</th>
<th>Rate – controlling process</th>
</tr>
</thead>
<tbody>
<tr>
<td>D1</td>
<td>(\alpha^2)</td>
<td>One dimensional diffusion</td>
</tr>
<tr>
<td>D2</td>
<td>(\alpha + (1-\alpha) \ln (1-\alpha))</td>
<td>Two dimensional diffusion</td>
</tr>
<tr>
<td>D3</td>
<td>([1-(1-\alpha)^{1/3}]^2)</td>
<td>Three dimensional diffusion - Spherical symmetry - Jander equation</td>
</tr>
<tr>
<td>D4</td>
<td>([1-(2/3)\alpha] - (1-\alpha)^{3/3})</td>
<td>Three dimensional diffusion - Spherical symmetry – Ginstling - Brounshtein equation</td>
</tr>
<tr>
<td>F1</td>
<td>(-\ln (1-\alpha))</td>
<td>Random nucleation - one nucleus on each particle - Mampel equation.</td>
</tr>
<tr>
<td>A2</td>
<td>([-\ln (1-\alpha)]^{1/2})</td>
<td>Random nucleation – Avrami equation. I</td>
</tr>
<tr>
<td>A3</td>
<td>([-\ln (1-\alpha)]^{1/2})</td>
<td>Random nucleation – Avrami equation II</td>
</tr>
<tr>
<td>R2</td>
<td>(1-(1-\alpha)^{1/2})</td>
<td>Phase boundary reaction - Cylindrical symmetry</td>
</tr>
<tr>
<td>R3</td>
<td>(1-(1-\alpha)^{1/3})</td>
<td>Phase boundary reaction - Spherical symmetry</td>
</tr>
</tbody>
</table>
### Table 2.3 The kinetic models of decomposition

<table>
<thead>
<tr>
<th>No.</th>
<th>$g(y) = k \times \tau =$</th>
<th>Notes</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td>Nucleation and nucleus growing</td>
</tr>
<tr>
<td>1</td>
<td>$[-\ln(y)]^{1/4}$</td>
<td>$n = 1/4$ (plate)</td>
</tr>
<tr>
<td>2</td>
<td>$[-\ln(y)]^{1/3}$</td>
<td>$n = 1/3$</td>
</tr>
<tr>
<td>3</td>
<td>$[-\ln(y)]^{1/2}$</td>
<td>$n = 1/2$</td>
</tr>
<tr>
<td>4</td>
<td>$[-\ln(y)]^{2/3}$</td>
<td>$n = 2/3$</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Phase boundary reaction</td>
</tr>
<tr>
<td>5</td>
<td>$1 - y$</td>
<td>$n = 1$</td>
</tr>
<tr>
<td>6</td>
<td>$1 - y^{1/2}$</td>
<td>$n = 2$ (cylinder)</td>
</tr>
<tr>
<td>7</td>
<td>$1 - y^{1/3}$</td>
<td>$n = 3$ (sphere)</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Diffusion</td>
</tr>
<tr>
<td>8</td>
<td>$(1 - y)^{2/3}$</td>
<td>$n = 3/2$</td>
</tr>
<tr>
<td>9</td>
<td>$[\gamma \ln \gamma + (1 - \gamma)]/4$</td>
<td>$n = 2$ (cylinder)</td>
</tr>
<tr>
<td>10</td>
<td>$\sqrt{2} - (1 - \gamma)/3 - \gamma^{2/3}/2$</td>
<td>$n = 3$ (sphere)</td>
</tr>
<tr>
<td>11</td>
<td>$(1 - y^{3/2})^2$</td>
<td>Jander's type</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Power law</td>
</tr>
<tr>
<td>12</td>
<td>$(1 - y)^{1/4}$</td>
<td>$n = 1/4$</td>
</tr>
<tr>
<td>13</td>
<td>$(1 - y)^{1/3}$</td>
<td>$n = 1/3$</td>
</tr>
<tr>
<td>14</td>
<td>$(1 - y)^{1/2}$</td>
<td>$n = 1/2$</td>
</tr>
<tr>
<td>15</td>
<td>$(1 - y)^{3/2}$</td>
<td>$n = 3/2$</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Chemical reaction</td>
</tr>
<tr>
<td>16</td>
<td>$-\ln(y)$</td>
<td>$n = 1^{st}$ order</td>
</tr>
<tr>
<td>17</td>
<td>$1/\gamma - 1$</td>
<td>$n = 2^{nd}$ order</td>
</tr>
<tr>
<td>18</td>
<td>$(1/\gamma^2 - 1)/2$</td>
<td>$n = 3^{rd}$ order</td>
</tr>
</tbody>
</table>