1.0 Introduction

The basic aim behind development of any drug delivery system (DDS) is to achieve a safe and effective therapy for the human being. For decades oral drug delivery become the major segment in the global pharmaceutical market. It is growing day by day because of being a favorite route for drug administration (Tiwari et al. 2008).

A large number of developments in the field of pharmaceutical technology have made manufacturing of tablet a science. In recent days tablets become the most favourable dosage form as compare to other available dosage form (Rasenak et al. 2002). The popularity of this dosage form is because of advantages such as ease to manufacturing, convenience in administration, and high accuracy in dosage, stability and safety. Various method of manufacturing such as Wet, dry granulation and direct compression are the widely used methods for manufacturing of tablets (Shangraw, 1989; Rudnic et al. 2005).

1.1 Oral Drug Delivery

The majority of drug formulation administered orally in form of tablets, capsule, or liquid. The basic requirement of any delivery system is to make the effective absorption and release of drug to its absorption site in the GI tract. After effective absorption of drug to its absorption site, permeation or transportation of drug from an oral dosage forms into the general blood circulation (Laitinen, 2009).

There are various physicochemical properties such as solubility and permeability of active plays a major role in absorption of formulation. In recent development of new chemical entities (NCEs), more than 40% found the low solubility problem. This is the basic challenge during successful development of new formulation with effective
availability of drug to systemic circulation (Hauss 2007, Stegemann et al. 2007). Development of orally Rapid dispersible/dissolving tablets is an alternative solution to avoid the absorption of drug through GIT such as intraoral route. The drug can be directly administered to systemic circulation by using rapid release of drug in saliva and absorption of drug through oral mucosa (Seager 1998). But this dosage form required the effective and rapid release of drug in oral mucosa. The development of such formulation can be achieved by application of several physical and chemical techniques.

1.2 Introduction of Dispersible Tablet as a Dosage Form

Solid medicinal preparations have been used since antiquity (Griffenhagen, 1980). Initial references of tablets as dosage form can be found in Arabic Medical Literature, as per the references of Arabic medical sciences the active part of tablets (drug particles) were compressed between ebony rods and then tablets were manufactured by applying the hammer force. Details of the tabletting process were first published in 1843 when Thomas Brockendon was granted a patent for "manufacturing pills and medicinal lozenges by causing materials when in a state of granulation, dust or powder, to be made into form and solidified by pressure in dies." In 1895, an editorial in the Pharmaceutical Journal predicted, "tablets have had their day and will pass away to make room for something else." After a century, tablets are still the most popular dosage form because of their significant advantages and continuous development for the improvement and elimination of basic drawbacks and limitations of existing formulations.

Dispersible Tablets is an alternative to the traditional swallow tablet containing a special formulation, which will quickly disintegrate in water to form a suspension that can be drunk. It combines the ease of swallowing and the potentially improved bioavailability of a liquid formulation (Kovacic et al. 1989, Milovac et al. 1990, Macia et al. 1995), with the accurate dosing. Active ingredients unstable in aqueous solution may be stable as a dispersible tablet (Milovac et al. 1990). The dispersible tablet provides a utility dosage form, reducing the need for multiple formulations of the same drug. In the current world health economy, this reduces
development costs significantly. Today the pharmaceutical industry operates in an environment where containment cost and optimization of drug delivery must be considered along with efficacy and safety before a new drug product will be licensed (Morton, 1996). It is for this reason that the German Registration Authorities (BGA) has advocated the formulation of dispersible tablets.

1.2.1 Novel Concept of Dispersible Tablets as a Dosage Form

The tablets are still the most popular and accepted dosage forms due to its continuous development and implementation of innovative ideas to overcome the basic drawbacks of the existing formulations. The tablets and capsules considered as the most widely accepted dosage forms through Oral route of administration with proven advantages for decades, but it also have some drawback such as difficulty in swallowing as dysphasia is most common for pediatric, geriatric and bedridden patients. The novel concept of Rapid dispersible drug delivery system emerged from the desire to provide patient with conventional mean of taking their medication. Recently oral administration of formulation become most popular route of administration due to its ease of ingestion, pain avoidance, versatility and most importantly, patient compliance (Ghosh et al. 2005). Thus, a new drug delivery system known as Fast Dissolving/Disintegrating / melt-in-mouth tablets gaining importance by designing to be absorbed through the buccal and esophageal mucosa as the saliva passes into the stomach. In the latter case, the bioavailability of a drug from Rapid dispersible and or dissolving formulations may be even greater than that observed in conventional oral dosage forms (Anil et al. 2012).

On the basis of recent developments dispersible tablets can be distinguished in two forms: one which directly disintegrates or dissolves in the mouth without a need of drinking water and second which requires addition of water to form dispersion within seconds of time, and easy to taken by the patient. In both the cases, bioavailability of drug is significantly greater due to instant dispersion and solubility than those observed from conventional tablet dosage form (Simone et al. 2002).
1.2.2 Ideal Properties of Rapid Dispersible or Fast Dissolving Tablets (Gaurav et al. 2012)

A. Ideally Rapid dispersible tablets do not require water or less amount of water for oral administration, the formulation should be easily disintegrated or dissolve in oral cavity within a few seconds (Simone et al. 2002).

B. The formulation should have sufficient hardness and should be free from any friability problem to match the rigors of the manufacturing process and handling of finished product by target patient.

C. The drug loading capacity of rapid dispersible tablets should be high.

D. The formulation should have been free from any bitter or unpleasant taste with better organoleptic properties.

E. The formulation should be rapidly disintegrate or dissolve after oral administration in the oral cavity for rapid action.

F. It should be stable with low manufacturing cast and the process should be amenable to existing processing and packaging machineries.

G. It should be Cost-effective.

H. Avoidance of first pass effect which improves bioavailability of rapid dispersible tablets.

I. It should have more stability as compare to liquid dosage forms.

1.2.3 Problem Associated with Rapid Dispersible or Fast Dissolving Tablets

A. Drugs absorbed at specific site cannot be given in these dosage forms.

B. These tablets show high friability, less hardness than conventional tablets (Kaushik et al. 2004).

C. Drugs with relatively larger doses are difficult to formulate in to FDTs (Dutta et al. 2011).

D. Hygroscopic properties of formulation require extra moisture protection with special packaging for proper stability & safety of the products (Kumari et al. 2010).
1.2.4 Regulatory Aspects for the Novel Concepts of Dispersible Tablets

There are various novel concepts of dispersible tablets such as Dispersible tablets, Orodispersible tablets; Tablets for use in mouth, soluble tablets, Effervescent tablets, and Oral lyophilisates are official in European Pharmacopoeia. As per European pharmacopoeia soluble tablets are uncoated or film-coated tablets. They are intended to be dissolved in water before administration. The solution produced may be slightly opalescent due to the added excipients used in the manufacture of the tablets. As per European Pharmacopoeia Orodispersible tablets are uncoated tablets intended to be placed in the mouth where they disperse rapidly before being swallowed (European pharmacopoeia, 2010).

There are various dispersible tablets available in Indian Pharmacopoeia such as Dispersible Tablets, Soluble Tablets, and Tablets for use in mouth, and Effervescent Tablets. Indian pharmacopoeia defined dispersible tablets as uncoated or film-coated tablets that produce a uniform dispersion in water and may contain permitted flavorings and sweetening agents. (Indian Pharmacopoeia, 2010).

US FDA also recognized the concept of quick dissolving dosage forms and included orally disintegrating tablets (ODTs) in the Orange Book. Some of these dosage forms have been formulated to facilitate rapid disintegration and are manufactured by conventional means or by using Lyophilization or molding processes (USP 35-NF 30, 2012). As per the USNF disintegration time of tablets should not be more than one minutes (USP 35-NF 30, 2012).

1.3 Manufacturing of Rapid Dispersible Tablets

On the basis of recent developments the manufacturing of Rapid Dispersible Tablets, Fast Dissolving Tablets, and or Oral Dispersible Tablets can be divided in to two categories. First type’s involves manufacturing of tablets by conventional methods and later manufacturing of tablets with novel technologies (Parakh SR et. al. 2003).
1.3.1 Manufacturing of the Rapid Dispersible Tablets with Conventional Method

1.3.1.1 Direct Compression
Direct compression method is the most commonly used method of manufacturing for tablets. It is very cost effective and simple without any additional use of other equipments such as granulator and drying equipments (Shailesh et al. 2011).

1.3.1.2 By Granulation Method
The manufacturing of Rapid dispersible tablets or Fast dissolving tablets is also prepared by various granulation techniques such as wet granulation and dry granulation methods. Wet granulation is the most widely used process of granulation, involves wet massing of the powder blend with a granulating liquid containing a suitable binder, sizing of wet granules and drying of granules in a suitable dryer. The development of rapidly dispersible granules suitable for the formulation of ODTs has received a great interest (Okuda et al., 2009).

1.3.1.3 Lyophilization or Freeze-Drying
Lyophilization also known as Freeze-drying is the most widely used conventional manufacturing techniques for the formulation of rapid dispersible tablets. More than 40% of formulations of rapid dispersible tablets are manufactured with Lyophilization. In this process water is sublimed from the product after it is frozen. The various patented technologies of Zydus, Quicksolv and Lyoc technologies are based on the freeze drying of formulation for rapid disintegration. These technologies are basically used to manufacture ODTs.

1.3.1.4 Spray-Drying
Spray drying can produce highly porous and fine powders that dissolve rapidly. The formulations are incorporated by hydrolyzed and non-hydrolyzed gelatins as supporting agents, Mannitol as bulking agent, sodium starch glycolate or Croscarmellose sodium as disintegrating and an acidic material (e.g. citric acid) and / or alkali material (e.g. sodium
bicarbonate) to enhance disintegration and dissolution. Tablet compressed from the spray
dried powder disintegrated within 20 seconds when immersed in an aqueous medium
(Reddy et al. 2002).

1.3.1.5 Tablet Moulding
Moulding process is of two type’s i.e. solvent method and heat method. Solvent method
involves moistening the powder blend with a hydro alcoholic solvent followed by
compression at low pressures in molded plates to form a wetted mass (compression
moulding). The solvent is then removed by air-drying. The tablets manufactured in this
manner are less compact than compressed tablets and possess a porous structure that
hastens dissolution (Wehling et al. 1996).

1.3.1.6 Sublimation
The slow release profile of the compressed tablet containing even highly water-soluble
diluents and excipients is basically due to the fact that the low porosity of the tablets
reduces water penetration into the matrix. The incorporation of volatile materials during
formulation of tablets using the conventional method resulting in highly porous
structures, which can be easily removed by sublimation (Figure – 1.1) (Shailesh et al.
2011).

1.3.1.7 Fast Dissolving Films
Fast dissolving concept is the new concept for the formulation of rapid disintegrating
formulation. In this technique, active is mixed with water soluble polymer and other taste
masking ingredients, this mixture is disperse in evaporative solvents and then allowed to
form a film (Bess et al. 2006, Shailesh et al. 2011).

1.3.1.8 Mass-Extrusion
Mass extrusion involves softening the active blend using the solvent mixture of water
soluble polyethylene glycol, using methanol and expulsion of softened mass through the
extruder or syringe to get a cylinder of the product into even segments using heated blade to form tablets. (Makino et al. 1993).

![Figure 1.1: Method of Sublimation](image)

### 1.3.2 Manufacturing of Rapid Dispersible or Fast Dissolving Tablets by Novel Technologies

- Zydis Technology
- Durasolv Technology
- Orasolv Technology
- Lyoc Technology
- Flash Dose Technology
- Wowtab Technology
- Flash tab Technology
- Dispersible Tablet Technology
- Pharmaburst Technology
1.4 Current Status of Rapid Dispersible Formulations in India

There are various formulations based on fast dissolving or rapid dispersible tablets from various therapeutic segments available in Indian market (Table 1.1). But the growth of fast dissolving tablets is still in its initial phase. Recent market survey shows a positive sign in favor of rapid disintegrating formulation, more than a half of patients prefer ODTs to other dosage forms (Deepak K., 2004, Tarique et al. 2011).

1.5 Basic components of Rapid Dispersible Tablet Formulation

1.5.1 Drug

High dose drugs which are highly water soluble, poorly compressible and hygroscopic pose the greatest difficulty in a dispersible tablet formulation. Excipients must be carefully selected to produce a tablet matrix with high compressibility and low aqueous solubility and hygroscopicity.

<table>
<thead>
<tr>
<th>Brand Name</th>
<th>Strength</th>
<th>Active Ingredients</th>
</tr>
</thead>
<tbody>
<tr>
<td>Imodium Lingual</td>
<td>2 mg</td>
<td>Imodium</td>
</tr>
<tr>
<td>Mosid – MT</td>
<td>2.5 mg / 5.0 mg</td>
<td>Mosapride citrate</td>
</tr>
<tr>
<td>Nimulid – MD</td>
<td>50 mg / 100 mg</td>
<td>Nimesulide</td>
</tr>
<tr>
<td>Claritin Reditab</td>
<td>5 mg / 10 mg</td>
<td>Loratidine</td>
</tr>
<tr>
<td>Feldene Melt</td>
<td>10 mg / 20 mg</td>
<td>Piroxicam</td>
</tr>
<tr>
<td>Maxalt-MLT</td>
<td>5 mg / 10 mg</td>
<td>Rizatriptan</td>
</tr>
<tr>
<td>Pepcid RPD</td>
<td>20 mg / 40 mg</td>
<td>Famotidine</td>
</tr>
<tr>
<td>Zyprexa Zydis</td>
<td>5 mg / 10 mg / 20 mg</td>
<td>Olanzapine</td>
</tr>
<tr>
<td>Zofran ODT</td>
<td>4 mg / 8 mg</td>
<td>Ondansetron</td>
</tr>
<tr>
<td>Remeron Soltab</td>
<td>15 mg / 30 mg / 45 mg</td>
<td>Mirtazepine</td>
</tr>
</tbody>
</table>
1.5.2 Disintegrants
A disintegrants accelerates the rate at which a tablet breaks up in water. The current research will use so-called super disintegrants (Table 1.2), so-called because of high disintegrants efficiency attributed to their remarkable ability to absorb water and swell (Mitrevje & Hollenbeck, 1982). The schematic diagram for mechanism of disintegration is shown in Figure 1.2.

Table 1.2: List of Super Disintegrants

<table>
<thead>
<tr>
<th>Super disintegra nt</th>
<th>Commercial variants</th>
</tr>
</thead>
<tbody>
<tr>
<td>Sodium Starch Glycollate</td>
<td>Primojel™, Explotab™</td>
</tr>
<tr>
<td>Cross-linked polyvinylpyrrolidone (Crospovidone)</td>
<td>Polyplasdone- XL™ , Kollidon-CL™</td>
</tr>
<tr>
<td>Cross-linked sodium carboxymethyl cellulose (Croscarmellose)</td>
<td>AC-Di-Sol™, CLD™</td>
</tr>
<tr>
<td>Low substituted carboxymethyl cellulose</td>
<td>Nymcel-ZDIO™, Nymcel-ZD16™</td>
</tr>
<tr>
<td>Polacr in Potassium</td>
<td>Amberlite IRP88™</td>
</tr>
</tbody>
</table>

1.5.3 Binder
The binder and solvent in wet granulation have a profound effect on the disintegration properties of the tablet (Table 1.3). The aqueous solubility of the binder will affect tablet disintegration properties, and this is well documented (Holstius & Dekay (1952).

Table 1.3: List of Water soluble Binders

<table>
<thead>
<tr>
<th>Binder</th>
<th>Commercial Variants</th>
</tr>
</thead>
<tbody>
<tr>
<td>Hydroxyethylcellulose</td>
<td>Natrosol™</td>
</tr>
<tr>
<td>Hydroxypropylmethylcellulose</td>
<td>Methocel™</td>
</tr>
<tr>
<td>Hydroxyethyl Methylcellulose</td>
<td>Walocel™</td>
</tr>
<tr>
<td>Sucrose</td>
<td>Demarara Sugar™</td>
</tr>
<tr>
<td>Polyvinylpyrrolidone</td>
<td>Plasdone™</td>
</tr>
</tbody>
</table>
1.5.4 Diluents

A diluents or filler facilitates the compression of a formulation and gives tablet strength and acceptable appearance. Diluents can be broadly categorized by their aqueous solubility and choice is dependent on the physico-chemistry of the drug; solubility, hygroscopicity, compression properties, instability and the method of manufacture. Diluents used in dispersible tablet formulations are listed in Table 1.4.

**Table 1.4: List of Diluents and Fillers**

<table>
<thead>
<tr>
<th>Water insoluble</th>
<th>Partially soluble</th>
<th>Water soluble</th>
</tr>
</thead>
<tbody>
<tr>
<td>Calcium carbonate</td>
<td>Pre-gelatinized starch</td>
<td>Dextrose</td>
</tr>
<tr>
<td>Calcium phosphates</td>
<td>Low-substituted Hydroxypropyl cellulose</td>
<td>Lactose</td>
</tr>
<tr>
<td>Magnesium carbonate</td>
<td></td>
<td>Mannitol</td>
</tr>
<tr>
<td>Microcrystalline cellulose</td>
<td></td>
<td>Sorbitol</td>
</tr>
<tr>
<td>Starch</td>
<td></td>
<td>Sucrose</td>
</tr>
</tbody>
</table>

1.5.5 Lubricants

Stearic acid salts, such as magnesium Stearate, are potentially unsuitable in dispersible tablet formulations because they are hydrophobic, and may form a scum giving an unpleasant appearance. Paradoxically most commercial dispersible tablets are lubricated using magnesium Stearate. Commonly used lubricants with their commercial grade are summarized in the Table 1.5.

**Table 1.5: List of Lubricants**

<table>
<thead>
<tr>
<th>Lubricants</th>
<th>Commercial Variants</th>
</tr>
</thead>
<tbody>
<tr>
<td>Magnesium Stearate</td>
<td>Hi – Mast™</td>
</tr>
<tr>
<td>Sodium Stearyl Fumerate</td>
<td>Lubripharm™</td>
</tr>
<tr>
<td>Polyethylene Glycol</td>
<td>Carbowax™</td>
</tr>
</tbody>
</table>
1.6 Process of Tablet Disintegration and Dissolution
Disintegration occurs when a tablet disrupts into fragments when brought into contact with fluid. This is followed by deaggregation, disintegration beyond the original granule size into the primary particles (Figure – 1.3). Dissolution occurs most rapidly from primary particles since the available surface area is large, but to a limited extent from the intact tablet, and the aggregates generated during tablet disintegration.

1.7 Basic Challenges in Formulation of Rapid Dispersible Tablets
The basic challenge during formulation design of Rapid dispersible Tablets or Fast dissolving tablets is the rapid disintegration and release of active to make more bioavailability of active into systemic circulation. The development of an ideal formulation for Rapid Dispersible Tablets is based on two major objectives,

1.7.1 Enhancement of Release Profile
Solubility of drug is the basic factor which controls the release profile of the finished product. There are various techniques available for the improvement of solubility and release profile of formulations. Particle size reduction or Micronization (e.g. by high pressure homogenization) might also increase the saturation solubility of a drug, further enhancing the dissolution rate. Dissolution rate of drug can be modified by modification of the solid state (polymorphs, pseudo polymorphs) of the active. Dissolution advantage due to different lattice energies of drug physical forms can be achieved by pseudo polymorphs. Dissolution modification can also achieve by modification of the solid state (amorphous forms) of active (Hancock et al, 2002).
Figure 1.2: Mechanism of Action of Strongly Swelling Disintegrants

- Water absorption of disintegrant particles at tablet surface
- Swelling of disintegrant particles
- Breakup of tablet surface structure.
- Chain reaction of absorption and disruption.
- Disintegration

Figure 1.3: Conceptual Diagram of Disintegration and Dissolution
1.7.2 Organoleptic Properties

Many drug substances are unpalatable and unattractive in their natural state (Miller & York, 1988). It is widely recognized that if a dosage form is unpalatable, patient compliance may be reduced, especially for long term treatment. Therefore, in dispersible tablet development, organoleptic properties are important. Flavors and sweeteners may be added to modify and mask taste. The dispersion produced by a tablet must have an acceptable mouth feel and this is related to the particle size and viscosity.

1.8 Literature Review

- **Verley et al. 1990** were studied the various dose of formulation details of lyophilized products; he suggested that formulation of high dosage is somewhat difficult with freeze drying method due to its fragile nature. Additionally, the formulation of very high dose actives is difficult. He reported that doses up to 125mg can be accommodated, but with higher doses it is more difficult to achieve dispersion.

- **Pebley et al. 1994** were invented the alternative method for removal of liquid by freeze drying technique to produce a rapidly dispersing tablet. It is claimed to have a lower porosity. Greater density and greater mechanical strength, while still disintegrating in normal amounts of saliva / aqueous solution. However, there is a possible explosive release of liquid from the material being dried, which may disrupt the structure of the material. For this reason, the process has previously been considered unsuitable for commercial production of well-formed shapes such as dispersible tablets. However, in the process described by Pebley, it is claimed that maintaining the temperature of the matrix during primary drying between the collapse temperature and the equilibrium freezing point, gave a satisfactory product.
• **Ishikawa et al. 1999** prepared and evaluated tablets containing bitter tasting granules masked by the compression method. Pirenzipine hydrochloride and oxybutynin hydrochloride were used as model drugs and Eudragit E-100, microcrystalline cellulose, hydroxypropylcellulose, and magnesium Stearate were used as excipients. The results showed that there was rapid in-vitro release of oxybutynin and pirenzipine at pH 1.2. The tablets disintegrated within 20 seconds into the saliva of the volunteers and they did not report a bitter taste after disintegration.

• **Pilgaonkar et al 2010** introduced the Rubi Oro dispersible technology for the development of Oro dispersible tablets of Acetaminophen. Paracetamol is very bitter having less solubility properties. The taste masking and solubility enhancement of drug with various soluble and insoluble polymers have been attempted for taste masking. Coating using water insoluble polymers particularly achieves the desired taste masking, but leads to retardation in drug release. On the basis of various formulation trials and studies he developed an environmental friendly aqueous coating system for taste masking whilst achieving at least 85% drug release in 15 mins. He used the desired particle size of Acetaminophen granules for the coating, and the granules were coated with aqueous coating system in a fluidized bed coater. Type of coating system and coating process as well as the coating level were optimized. The taste masked granules were further compressed into a rapidly disintegrating formulation using RubiODT technology with the help of extra granular ingredients such as Pan Excea ODT, disintegrants, flavors, sweeteners etc. The developed formulation was evaluated for including in-vitro dissolution rate, wicking time, disintegration time and mouth-feel.

• **Channer et al. 1986** were studied the shape and surface dimensions of tablets have a significant impact on transit time through the esophagus. For psychological reasons, patients tend to find long, thin formulations such as oval tablets easier to swallow. Significantly reduced esophageal transit times compared with round
tablets of equal weight was demonstrated. Tablet surfaces with a high water adsorption capacity can also increase adherence to the esophageal mucosa and increase transit times, especially if ingested with too little water.

1.9 Objectives of Study

The main aim of this study is to develop new concept for the formulation of rapid dispersible tablets or Fast dissolving tablets using novel concepts such as solubility enhancement of active for fast and better release of drug to achieve better bioavailability of active in vivo, taste masking of active with various techniques to improve organoleptic properties and patience compliance. The design of formulation was basically developed for the pediatric and geriatric patient. The project was investigated the formulation of two classes of drugs that are potentially difficult to formulate as rapid dispersible tablets: high dose, poorly compressible drugs, with low aqueous solubility, and medium dose, highly insoluble drugs. Paracetamol and Tolfenamic Acid were used as models of each class respectively.

There are various dosage form of individual Paracetamol such as conventional tablets, dispersible tablets, effervescent tablets, etc available in the Indian and international market. Fixed dose combination such as Paracetamol and Ibuprofen, Paracetamol and Diclofenac Sodium, Paracetamol and Ketoprofen etc are also available in the market (IDR Compendium, 2009). The existing formulation with Ibuprofen, Diclofenac sodium is having common side effect such as gastric irritation, nausea, and vomiting in some case. The basic drawback of Paracetamol dispersible tablets is the bitter taste of formulation instead of presence artificial sweetener in the formulation; this is basically due to property of Paracetamol. The existing marketed formulation still requires developing with better release and organoleptic properties.

Tolfenamic acid (TA) is classified as non-steroidal anti-inflammatory drugs (NSAIDs). It is basically used in the treatment of migraine. A study concludes that use of Tolfenamic Acid was significantly reduced the further side effect of other drugs of same therapeutic
class such as nausea, vomiting, irritation, tremor, thirst and dryness of mouth (Kim Vilbour et. Al: 1989, Niopas I et. Al: 1995). On the basis of literature and market survey it was observed that still it is rare to find any suitable fast dissolving formulation for Tolfenamic Acid, so there is need to develop a formulation with effective taste masking (IDR Compendium, 2009).

1.10 Rational of Research Work

The proposed work aim to improve the release profile of drug to make formulation more bio available and taste masking of active to make easy to administration in case of pediatrics. The basic work summarized as,

- Drug Profile
- Preformulation studies and characterization of actives
- Application of Co-micronization as novel concept in formulation of insoluble drugs
- Application of dual technologies of solid dispersion and polymer coating in formulation of insoluble and bitter drugs
- Novel concept of FDCs for development of rapid dispersible dosage forms
- Organoleptic evaluation and stability of formulations

The Research Strategy is rationalized as follows:

Chapter Two: The research work was initiated with the brief study of drug profile used during formulation of rapid dispersible tablets.

Chapter Three: Investigated the preformulation studies of different formulation of Tolfenamic acid, Paracetamol, and Tolfenamic Acid and Paracetamol (FDCs), characterization of both actives also investigated in the given section.

Chapter Four: Investigated the solubility enhancement of Tolfenamic Acid using co-micronization approach for rapid release profile of formulation. The effect of particle size, surfactants, co micronization of active with surfactant on release profile was
investigated during study. Stability study of optimized formulation also evaluated to check the impact of temperature and humidity for specified durations.

Chapter Five: Investigated the influence of granule size and intra-granular disintegrants type on tablet properties, particularly dispersion and wetting characteristics of formulation.

Chapter Six: Investigated the solubility enhancement of Paracetamol using various approaches of solid dispersion methods for enhancement of release profile of active and formulation with suitable excipients. The taste masking of paracetamol was tried to mask with application of polymer coating. Implementation of dual technology in a single formulation was investigated to check the release kinetics and taste properties of formulation.

Chapter Seven: Concept of fixed dose combination was investigated in formulation of dispersible tablets. Combination of Tolfenamic acid and paracetamol was tried to optimized for the effective treatment of migraine in pediatrics. The formulation was also evaluated organoleptically for better patient compliance. Stability study of optimized formulation was also evaluated as per ICH guidelines.

Chapter Eight: The summary of research findings by implementation of various technologies was discussed in the given section. The future directions for the advancement of formulation also summarized in the given section.