SUMMARY, CONCLUSION AND RECOMMENDATIONS

The thesis describes Design and Evaluation of Orodispersible tablets of Anti-inflammatory and Anti-emetic drugs with Superdisintegrants. The thesis consists of 09 Chapters.

Objectives of the investigation and introduction to ODTS are described in Chapter-I. Aceclofenac and Paracetamol widely prescribed anti inflammatory drugs and exhibit low and variable oral bioavailability due to their poor aqueous solubility. Similarly Ondonasetron and Metaclopramide are widely prescribed anti-emetic drugs exhibiting variable oral bioavailability. They are practically insoluble in water and aqueous fluids. The above drugs requires enhancement in solubility for increasing their oral bioavailability. Among the various approaches ODTS has gained good acceptance in recent years in pharmaceutical industry for enhancing the solubility of poorly water soluble drugs. Superdisintegrants also have ability to increase the solubility of lipophilic water-insoluble drugs by reduction in disintegration time. Though ODTS and use of superdisintegrants for enhancing the solubility and absorption of poorly water soluble drugs have been investigated individually, no reports are available on their combined use in enhancing the solubility and absorption rate. In the present investigation Aceclofenac, Paracetamol separately and in combination of ACE with PCT were tried to enhance the solubility, rapid onset of action, absorption rate and bioavailability using superdisintegrants.
The major objective is to evaluate the rapid onset of action in case of patients suffering from dysphagia especially in pediatrics, geriatrics and mentally challenged patients. By formulating ODTS with superdisintegrants such as crosscarmellose sodium, primojel, Isapgol husk, cross linked tragacanth, sodium starch glycolate and Cross povidone. The other objectives include: to evaluate the drug excipients interaction study by FTIR and DSC. Precompression studies includes Angle of repose, Hausner’s ratio, swelling index and compressability index. Post compression parameters such as hardness, friability, weight variation, wetting time, wetting volume, drug content uniformity, test for dispersion, water absorption ratio, \textit{in-vitro} disintegration and \textit{in-vitro} dissolution studies. The pore formation by sublimation method were studied by SEM. In preclinical studies the antiinflammatory activity was carried out using carrageenan induced rat paw edema method for Aceclofenac ODTS, pure Aceclofenac, combined aceclofenac and paracetamol ODTS and to evaluate the stability of selected ODTS.

Review of the drugs selected and excipients used is given in Chapter II. Design and evaluation of Aceclofenac and paracetamol ODTs in separate and in combined by direct compression method was explained in Chapter III. Design and evaluation of ODTS of Ondensetron hydrochloride by direct compression and sublimation method was described in Chapter IV. Design and evaluation of ODTS of Metaclopromide hydrochloride by direct compression and sublimation method was described in chapter V. Analytical methods used in the study are described in Chapter III, IV and V a U.V. Spectrophotometric methods were used for estimation of Aceclofenac Paracetmol, Ondensetron Hydrochloride and Metaclopramide in \textit{in vitro} studies.
Chapter 3

All the individual formulations of aceclofenac odfs, paracetamol odfs and combined formulations of aceclofenac and paracetamol odfs were described in chapter 3 and formulated by direct compression method which is simple and economical, different superdisintegrants were used in different ratios among them cross linked tragacanth was optimized in lab. cross linked tragacanth was prepared by using epichlorhydrin. The effects of ratio of tragacanth to epichlorhydrin, temp and time of reaction were studied. Based on the results of intrinsic properties, optimum conditions for cross linking of tragacanth was found at temp 105°C, time 45min and 1:0.8 ratio of tragacanth and epichlorhydrin.

Precompression evaluation parameter indicates good flow property, good compatibility and compressibility index were within the range.

Aceclofenac odfs-10-12.5%

Paracetamol odfs-12-17.4%

Combined aceclofenac and paracetamol odfs 11.1 to 16.43%.

Post compression evaluation parameters such as hardness was found to be 2.5 to 3.6 kg/cm. It shows good mechanical strength, friability was found well within the range not less than 1%. the weight of all formulations was found to be uniform. The drug content uniformity was performed for all the formulations and found to be uniform.

The hydrophilicity of the formulations was checked by wetting time. The odfs containing cross linked tragacanth showed faster wetting time compared to odfs.
containing CCS, SSG and Cross povidone. Wetting volume of FAP8 was found to be least that is 2.2ml.

Odis containing CLT showed faster swelling action when compared to odts containing CCS, SSG and Cross povidone. As the concentration of CLT was increased the water absorption ratio get increased due to more swelling and wicking action.

*Invitro* disintegration time for all formulations found to be as follows CLT< Cross povidone < CCS < SSG. The least disintegration time was found to be FAP8 formulation containing 4% CLT and time 28sec.

This is due to quicker hydration and higher swelling property. *Invitro* drug release the series of the best formulation is as follows FAP8 >FAP12>FAP5>FAP2. FAP8 shows maximum drug release.

Chapter 4

Design and evaluation of ODTs of Ondansetron HCL was described in chapter 4. Ondansetron HCL odt was formulated by two methods a) Direct compression  b) Sublimation method by using various superdisintegrants like CCS, Primojel, Isaphgol husk. Camphor is used as subliming agent in sublimation technique. Pre and Post compressional evaluation parameters was found to be within limit.

Formulation containing Isaphgol husk showed least wetting time is the DCI3 showed 39sec and SBI3 showed 35sec this is due to high wicking and swelling property. Tablets prepared with 10% Isaphgol husk and 10% camphor showed least disintegration time 15sec compared to all other formulation’s, this is because of the
method of formulation of odt's, high swelling power and wicking property of Isapgol husk. The maximum drug release for the directly compressible tablets with superdisintegrants CCS, Primojel and Isapgol husk was found to be 93.56%, 91.33%, 96.37% respectively. The maximum drug release for the sublimed tablets with CCS, Primojel and Isaphgol husk were found to be 96.56%, 94.68% and 98.89% respectively.

The rate of drug release of formulation prepared by sublimation method was greater than the rate of drug release of formulation prepared by direct compression method. This is due to the Orodispersible structure which helps for the penetration of dissolution medium into the pores of tablets formed upon sublimation of camphor which facilitate quick and complete disintegration.

The formulations with Isapgol husk showed higher % drug release compared to CCS and Primojel. The rapid disintegration and dissolution of formulation with Isapgol husk shown better drug release.

Chapter 5

Chapter 5 describes the design and evaluation of Metoclopramide HCL Odts by direct compression and sublimation method with the combination of super disintegrants. All the formulation were subjected for pre and post compressional evaluation parameters.

Disintegration study showed that the disintegrating time of the tablets decreased with increase in the concentration of the super disintegrates upto optimum concentration 4% SSG, 6% Cross povidone, 20% Camphor.
Metaclopramide ods with combination of superdisintegrants such as 4% SSG, 6% Cross povidone, 20% Camphor prepared by sublimation method showed least disintegration time 13 sec. This is due to pore formation which is confirmed by SEM studies.

Maximum drug release for the directly compressed tablets with combination of SSG (4%) and Crosspovidone(6%) found to be 99.36% at the end of 12 mins. The maximum drug release for the sublimed tablets with combination of SSG and crosspovidone was found to be 96.05% at the end of 6 mins. This was due to their low hardness and porous structure which helps for penetration of dissolution medium into the pores of tablets formed upon sublimation of camphor which facilitates quick and complete disintegration.

Chapter 6

Chapter 6 describes stability studies and in vivo studies. Stability studies was carried only for the selected formulation FAP8, SBC2, MS3 as per ICH guidelines. Drug content and dissolution profiles of the tablets remained unchanged after storage for 3 months at 40°±2° c and 75±5% RH. Drug release profile also remained unchanged during the storage period for all the drugs such as Aceclofenac, Paracetamol, Ondansetron Hcl and Metoclopramide.

The in vivo a pre clinical study was carried out by Carrageenan induced rat paw edema method using plethysmograph. The anti-inflammatory activity shown by Odts such as FAP7, FA3, FAP8 were comparable with the standard drug.
Hence a combination of drugs such as (aceclofenac and paracetamol) odt's formulated by direct compression by using superdisintegrants is a innovative work shall be recommended for enhancing the rate of disintegration, therapeutic activity, dissolution and bioavailability. The method is simple and economical. Combination of superdisintegrants 4% SSG and 6% cross povidone in the metaclopramide odt's by sublimation method showed best results. The taste masking of a bitter drug ondansetron is also possible, hence patient compliance shall be enhanced by formulating the ODTs.