CHAPTER 6
SUMMARY, CONCLUSION AND RECOMMENDATIONS

The utilization of plant based gums turns out to be imperative as pharmaceutical excipient, especially in designing of control drug delivery system. Natural polymers, have advantage over synthetic and semi-synthetic polymers, as they were easily available, economical, non-irritant, biodegradable, biocompatible and eco-friendly.

Considering the applicability of natural gums, the present research envisages to demonstrate the utilization of Okra gum (OG) in development of gastro retentive drug delivery system.

6.1 SUMMARY

Chapter 1
- Chapter-1 describes about the general introduction and background regarding different types of gastro retentive drug delivery systems and significance of natural gums in the development of several pharmaceutical dosage forms.

Chapter 2
- Chapter-2 discuss about the detailed literature review on development of different drug delivery systems of repaglinide. Literature on floating DDS, mucoadhesive DDS and okra gum was also discussed.

Chapter 3
- The aim and objectives of the present study were discussed in chapter-3. The work in different phases were under taken is explained.

Chapter 4
- Various materials and their sources were given in Chapter-4. Drug profile (repaglinide), polymer profiles and list of instruments were discussed.
- Complete methodology for experimental works on okra gum, optimization of floating tablets and formulation of mucoadhesive tablets using thiolated okra gum were discussed.

Chapter 5
- Okra gum (OG) was extracted from fresh unripe fruits of Abelmoschus esculents and studied for different physicochemical and phytochemical properties.
OG was found to be stable throughout the study period of 6 months.

FTIR and DSC studies confirms the compatibility of excipients with the drug.

Repaglinide floating tablets were developed by using 3-full level factorial design using naturally occurring plant based polymers along with combination of synthetic polymer.

The effect of interaction of three dependent variables on two responses were studied and optimized. This study concluded that all three variables had significant effect on selected responses.

Optimum concentrations of okra gum, HPMC K15M and xanthan gum were found to be 32.93%, 15% and 13.91%.

By using optimized concentrations, formulation(ORF-1) was prepared and evaluated for in vitro floatability and in vivo studies.

Anticipated results were relatively comparable to the experimental results which illustrates the preciseness of the design.

The drug release profile of ORF-1 follows diffusion as well as erosion mechanism (n value for peppas model-0.6979).

In vivo buoyancy study of ORF-1 provided the evidence that tablets floated on the gastric fluid but did not adhere to gastric mucosa.

In vivo release studies confirms that there is decline in the $K_a$ and $K_e$ by formulating into gastro retentive drug delivery system, which is desirable for control release and ability to alter pharmacokinetic behaviour in the desirable mode.

A strong linear relationship was observed between fraction of drug released and fraction of drug absorbed with regression value of 0.9708.

Formulation was found to be stable without any significant change under different storage conditions.

OG was evaluated for mucoadhesion potential, the result shown that mucoadhesive strength of okra gum was comparable to carbopol but lesser than sodium alginate under the experimental conditions used in this study.

OG bears good mucoadhesion property, but there is a need to enhance mucoadhesion potential by suitable approaches such as thiolation etc., to employ in mucoadhesion drug delivery systems.
Thiolation of OG was achieved by esterification with TGA.

TOG was further characterized by FTIR, DSC and SEM analysis.

Mucoadhesion potential of TOG was evaluated, compared at two different concentrations with OG and sodium alginate by formulating repaglinide mucoadhesive tablets.

Improved mucoadhesion potential of TOG in contrast to others can be attributed to the formation of strong disulfide bond with mucus.

In vitro dissolution studies were further carried out by paddle method and modified method to mimic the in vivo adhesion of dosage form.

From $f_2$ and $f_1$ values, one can conclude that modified basket method was signified with the paddle method, but with low $f_2$ (64.05-70.37) and high $f_1$ values (7.08-10.63).

Thiolated formulations shown diffusion and swelling release mechanism (n value was found to be in between 0.7548 to 0.8844) except RGM-6B (n value-0.9118).

$r^2$ values for zero order were seen in vicinity of 0.9759 and 0.9987, affirming the closeness to the fulfilment of a perfect zero order kinetics.

Thiolated formulation (RGM-6) was able to withstand peristaltic movements of GIT up to 8 h, as it forms strong disulfide bond with the mucus.

Bioavailability studies confirms that there is decline in the $K_a$ and $K_e$ and enhanced half life by formulating into gastro retentive drug delivery system.

Stability studies conducted for RGM-6 formulation confirms that the product was found to be stable without any significant changes in its properties.

### 6.2 CONCLUSION

OG was proved as non toxic, compatible and has the potential application in designing of floating drug delivery system. Thiolation of OG was achieved by esterification with TGA. Formulated repaglinide gastro retentive mucoadhesive tablets were shown enhanced mucoadhesion potential by 2-3 folds as a result of thiolation. All these features makes thiomers as new promising excipient for mucosal delivery.

In vivo release studies for both ORF-1 and RGM-6 confirms that there is decline in the $K_a$ and $K_e$, which is desirable for control release and ability to alter
pharmacokinetic behaviour in the desirable mode by formulating into GRDDS. Thus the use of plant based polymers can be a good replacement for synthetic polymers in the development of controlled release dosage forms.

6.3 RECOMMENDATIONS

- Laboratory formulations needs the scale up studies to meet the industrial requirements.
- The optimized formulations have shown very encouraging buoyancy and bioavailability results in animal studies. This work should be extend to human volunteers to confirm the clinical efficacy of developed drug delivery systems (floating and mucoadhesive DDS), which may be require further modifications.
- Extracted OG can be studied further to know its effectiveness in the development of several novel drug delivery systems such as in situ gel, transdermal patches and microspheres etc.