ABSTRACT SUMMARY
A controlled release, patient-friendly orally disintegrating tablet using controlled release micro granules of a water soluble compound, Propranolol HCl, was developed. The study was aimed at the evaluation of the compression characteristics of the extended release pellets using various orally disintegrating matrices and the study of release profiles using standard mathematical models.

INTRODUCTION
Tablets that disintegrate rapidly in the mouth are convenient for patients who have difficulty in swallowing conventional oral dosage forms. Although various manufacturing technologies such as freeze-drying \(^1\), tablet molding \(^2\), disintegrant addition \(^3\), spray-drying \(^4\), and sublimation \(^5\) have been studied, rapidly disintegrating tablets that are superior in both pharmaceutical function, for example, sustained-release and enteric dosage forms, and for the ease of swallowing have rarely been reported. Propranolol HCl, a non selective Beta adrenergic blocking agent, was selected as a model drug which is used in divided daily doses for the long term treatment of heart disease \(^6\). Propranolol is marketed as a capsule containing extended release coated granules, but some patients may find capsules difficult to swallow due to their size. Therefore the purpose of this study was to develop a patient-friendly, extended release, orally disintegrating tablet of Propranolol manufactured using conventional processing technology. The ODT composition consisted of extended release, coated micro granules and inactive granules. The coated pellets were formulated with an in house ODT composition containing Mannitol, microcrystalline cellulose, low-substituted hydroxypropyl cellulose (L-HPC), colloidal silicon dioxide, crospovidone, and two different commercially available ODT compositions, Parteck®ODT and Pharmaburst @500. Compression properties of OD Tablets, such as the tensile strength, disintegration time, and dissolution of the drug from extended release pellets using USP type 2 dissolution methods were evaluated.

EXPERIMENTAL METHODS
The extended release pellets were manufactured by coating core pellets manufactured by extrusion and spheronization. A wet mass of Propranolol HCl and microcrystalline cellulose PH 101 was made using low shear granulator. The wet mass was extruded using a Luwa extruder and the extrudates are spheronized using a Luwa spherizer. The resultant pellets were tray dried and the dried pellets were sieved through 25 mesh and 30 mesh screens. Pellets that passed through the 25 mesh screen and retained on the 30 mesh screen were taken for the study.

The pellets were coated with Eudragit NE 30 D with talc as anti-tacking agent in a fluid bed coater. A portion of coated pellets were blended with L- HPC, crospovidone, MCC, colloidal silicon dioxide, and mannitol and compressed on a single station compression machine into tablets. Similarly, a second portion of extended release pellets were blended using Parteck®ODT and a third portion with Pharmaburst @500. The tablets were prepared using a single station compression machine. The extended release pellets and ODT tablets made with three compositions were evaluated for drug release using the USP Type 2 dissolution method. In addition ODT tablets were evaluated for tensile strength and USP disintegration. The dissolution data were fitted into zero-order, first-order, Higuchi and Hixson-Crowell models to identify the release kinetics and mechanism of drug release.
RESULTS AND DISCUSSION
A 24 hour release profile was obtained on the pellets coated using Eudragit NE 30 D coating polymer to a weight gain of 25% w/w. The comparative dissolution profiles of Propranolol HCl Eudragit NE 30 D coated pellets, and in-house tablets containing 25% w/w coated beads blended with mannitol/ L-HPC, Pharmaburst ®500, and Parteck®ODT are shown in figure 1. The drug dissolution profiles of multiple-unit tablets and coated pellets were found to be closely similar, indicating that the integrity of pellets remained unaffected to a greater extent during the compression process. The target hardness was 5 kPa and the USP disintegration time was less than 25 seconds for all compositions. The tablets manufactured at increased compression forces resulted in harder tablets with resulting hardness in the range of 8-10 kPa. However, the dissolution of Propranolol was higher in these tablets indicating the fracture of multi units. The Pharmaburst ®500 and Parteck®ODT formulations performed comparatively better than the in-house mannitol/ L-HPC composition at higher hardness.

![Figure 1. Comparative Dissolution Profiles of Propranolol HCl Controlled Release ODT Tablets (Hardness-5kPa)](image)

Release profiles up to 14 hours have been used for the evaluation of the dissolution release kinetics using zero-order, first-order, and Higuchi and Hixson-Crowell models.

The in vitro release data for all compositions best described with First order and Higuchi’s mathematical expressions with resultant R² values greater than 0.95.

<table>
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<tr>
<th>Formulation</th>
<th>Zero Order R²</th>
<th>First Order R²</th>
<th>Higuchi Model R²</th>
<th>Hixson-Crowell Model R²</th>
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<tr>
<td>Parteck®ODT</td>
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<tr>
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</tr>
</tbody>
</table>

Table 1. R² values obtained from the Mathematical models for all compositions.

CONCLUSION
Modified-release multiple-unit orally disintegrating tablets were prepared successfully by compressing controlled release pellets containing propranolol hydrochloride as a model drug using an in house composition containing L HPC,MCC, Mannitol, colloidal silicon dioxide and crospovidone, as well as commercially available ODT compositions of Parteck®ODT and Pharmaburst®500. The drug release profile of the multiple-unit tablets was found to be closely similar to that of the multiple-unit capsules, indicating that compression did not alter the release profile of the drug from the coated pellets, and compression of controlled release pellets into an ODT composition is a viable formulation approach.

REFERENCES

ACKNOWLEDGMENTS
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