ABSTRACT
Telmisartan is an Anti-hypertensive drug which is insoluble in water; hence the drug may be slowly or incompletely dissolves in the gastro-intestinal tract. So the rate of Dissolution and therefore its bioavailability is less (bioavailability 42%). In the present Study an attempt has been made to prepare Fast Dissolving Capsules of Telmisartan by Using Super disintegrants- Crosspovidone, Ac-de-sol, and sodium starch glycolate, level of addition to increase the rate of drug release from dosage form to increase the dissolution rate and hence its bioavailability. The capsules were prepared by Dissolution methods and the prepared blend and capsules were evaluated for their physicochemical properties and In-Vitro dissolution study. The evaluation studies were performed such as Weight Variation, Thickness, Disintegrating Time, and In-Vitro Drug Release and Stability Study. The Disintegration time of Dissolving Capsules were increased by the addition of concentration of Superdisintegrants.

Keywords: Telmisartan, UV Spectroscopy, Sustained Release Capsule, Croscarmellose sodium.

INTRODUCTION
Telmisartan is used to treat high blood pressure (hypertension) by blocking the Hormone angiotensin thereby relaxing blood vessels, causing them to widen. High blood pressure reduction helps prevent strokes, heart attacks, and kidney problems. Telmisartan is an Angiotensin Receptor Blocker (ARB) shows high affinity for the angiotensin II type1 (AT1) receptors, has a long duration of action, and has the longest half-life of any ARB (24 hours)\(^1\). It is indicated for the treatment of hypertension but Telmisartan’s dual mode of action may provide protective benefits against the vascular and renal damage caused by diabetes and cardiovascular disease (CVD). It is practically insoluble in water and in the pH range of 3 to 9, sparingly soluble in strong acid (except insoluble in hydrochloric acid), and soluble in strong base. Numerous studies have been carried out in order to modify the dissolution kinetics of poorly soluble drugs to improve their bioavailability. A common method used to improve the dissolution rate of a poorly water soluble drug is by formation of a solid dispersion (SD) with hydrophilic polymer polyvinyl pyrrolidone and other diverse carriers\(^2\). Briefly, an SD is defined as a molecular mixture of drug in carriers. The changes of drug crystallinity to an amorphous form and the reduced particle size for better wettability are the main mechanisms whereby SD enhances drug dissolution\(^8\). The Bioavailability of Telmisartan is Poor About 45%, which due to Extensive First Pass hepatic metabolism; The Bioavailability can be increase by Fast Dissolving Formulation. Conventional Telmisartan tablets available in market are not suitable where quick onset of action is required\(^11\). Hence, the objective of the present study was to develop Telmisartan (SR) immediate release capsules and the main objective of the presents study was to develop Sustained release Capsules of Telmisartan by simple and cost effective direct compression methods.

MATERIALS AND METHODS
Telmisartan is procured by Lupin Drugs Pvt. Ltd. Pune, CrosscaromelloseSodium, Crosspovidone are gifted by Signet Chemical Corporation, Mumbai, Lactose,HPMC, PVG 6000, MCC pH 102, CCS PVP K 30 were procured by Debjit Bhowmik Etal, Colorcon Asia Pvt. Ltd. Mumbai.
Magnesium Stearate, is procured by Nice Chemicals Pvt. Ltd., Cochin.

**Preparation of sustained released Telmisartan Capsule by Dissolution Methods using Superdisintegrants**

CCS = Cros Carmellose Sodium  
MCC = Micro Crystalline Cellulose  
Average wt. of Telmisartan part: 140 mg

**PROCEDURE**

Telmisartan Sustained release Capsule was prepared by dissolving the Capsules in disintegration method using various Disintegrants used like Lactose Talc. Weighed the Telmisartan, PEG 6000, HPMC, MCC pH 102 according to the formula. Dissolve PEG 6000 & CCS in Ethanol by slow addition. Avoid lump formation during addition of PEG 6000 & CCS, stir to dissolve and to form a homogenous clear solution. Loaded the sifted material into the main bowl of Rapid Mixture and mix it for 5 mts. The formulations were shown in shown in table no.1.

**IN-VITRO DISSOLUTION STUDIES**

Dissolution studies were carried out as per the USP 26 specifications, using USP dissolution apparatus type 2 at pH conditions i.e. 6.8 Phosphate Buffer for 1 hr followed by the pH 6.8 for remaining hrs. Analysis Telmisartan was estimated by U.V.spectrophotometer at 223 nm. Best formulation was subjected to HPLC analysis as per the specifications given (Column used - Kromasil C 18 ODS column, Mobile Phase – Buffer : Acetonitrile – 75: 25 , pH of the mobile phase 3.0 (Adjusted with Orthophosphoric acid, Flow Rate - 1ml/min., Injection volume- 100µl, Wavelength – 215 nm, HPLC system – Waters). The prepared mobile phase was filtered through 0.45 mmicro pore filter and degassed by sonication for 10 minutes.

**BUFFER**

50 ml of 1 M monobasic sodium phosphate and 8.0 ml of 1 M phosphoric acid and dilute with water to 1000ml adjust with 1 M phosphoric acid to pH 3.0.

**STANDARD PREPARATION**

Weigh accurately about 100 mg of Telmisartan working standard in a 50ml Volumetric flask dissolves in a dissolution medium makeup the volume with same. Dilute 5 ml from the above solution to 50 ml with dissolution medium.

**PROCEDURE**

Inject 20 µl sample preparation (one injection) and standard preparation into the Liquid chromatography and record the chromatogram. Measure the responses for the major peaks. Calculate the dissolved quantity of Telmisartan in percentage form the peak areas of standard and sample preparation and percentage of potency of working standards used.

**ASSAY**

**Preparation of Standard Telmisartan (HPLC method)**

Weigh accurately about 50 mg of Telmisartan working standard in a 50ml volumetric flask dissolves in a dissolution medium makeup the volume with same. Dilute 5 ml from the above solution to 50 ml with dissolution medium.
Chromatographic condition
Mobile phase used for the analysis consist of Buffer: Acetonitrile aqueous solution in the ratio of 75:25 v/v. They were filtered before use through a 0.45 µm membrane filter and pumped through the column RP C18 (250 x 4.6 i.d) mm, 5µm, in isocratic mode at a flow rate of 1 mL/min. Prior to the injection of the drug solution, the column was equilibrated for at least 30 min with the mobile phase flowing through the system. The analysis was performed at ambient temperature and the run time was set at 10 min. The eluents were monitored at 223 nm and retention of Telmisartan was found to be 7.7 min.

Sample preparation
Weighed about 50mg equivalent of Telmisartan in a 100 ml volumetric flask and 5 ml of water, to disperse and 70 ml of methanol warm 10 minutes dilute to volume with methanol. Filter the supernatant liquid with 0.45 micron membrane filter. Dilute 5ml from the solution to the 50 ml with mobile phase.

Fourier transform infrared (FT-IR)
Fourier transform infrared (FT-IR) spectral studies were conducted on FTIR Spectrophotometer (Shimadzu Instrument Corporation Inc., Japan) instrument using KBr pellets to investigate possible interactions between the respective polymers in the release media. All samples were crushed with potassium bromide. The weight ratio of a sample and potassium bromide was 2 mg to 300 mg. Crushed powders were compressed using a hydraulic compactor at approximately 20,000 pounds under vacuum for 3 min. FT-IR measurements were performed under nitrogen atmosphere at a flow rate of 50 standard cubic feet per hour. Spectral scanning was conducted from 4000 to 400 cm−1 at a resolution of 4 cm−1.
Graph. 2: Telmisartan + Capsule Estimated by FTIR

STABILITY STUDY ON CAPSULES
The batch F1 are selected as an optimum batch and the stability study was carried out at accelerated condition of 40°C/75%RH condition for a period of three months.

Method
The capsules were individually wrapped using Aluminium foil and packed in ambered color screw cap bottle and put at above specified condition in incubator for 3 months. After three months capsules were evaluated for content uniformity and In-vitro drug release.

Observation
- The results of stability study after 3 months.
- The plot of cumulative % Drug release v/s Time.

Drug content
Comparative content uniformity of the Capsule after 3 months stability
Table 5: Stability Study Data of Formulation after Each Month at 40°C ± 2°C, 75% RH

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Graph. 3: Stability Study Data of Formulation after Each Month at 40°C ± 2°C, 75% RH

Table 5: Stability Study Data of Formulation After Each Month at 40°C ± 5°C, 75% RH

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RESULTS AND DISCUSSION
The procured sample of Telmisartan was tested for its identification by FTIR. The manufacturer was also confirmed of quality and purity of the sample. The drug and excipients compatibility was done physical and instrumental method at room temperature and refrigerator condition in opened and closed vial methods were used. The result does not show any physical or chemical change to the mixture after 14 days. This fact concluded that the drug and excipient are compatible with each other. Therefore the drug formulation of batch F1 was selected further encapsulated the granules into hard gelatin capsules in process evaluation and stability studies.

The F1 batch drug granules were encapsulated in hard gelatin capsules by using rotatory die process. They were evaluative for weight variation, disintegration, dissolution study. No significant difference was observed in the weight of individual hard gelatin capsules from the average weight. Hard gelatin capsules weights of all batches were found within recommended pharmacopeia limit. The data of uniformity of the content indicated that hard gelatin capsules add drug content with in pharmacopeia limits. The data of disintegration of the hard gelatin capsules shows within the pharmacopeia limits. The in vitro drug release of the hard gelatin capsules was done by using the type –ii USP paddle type operators and the in vitro % drug release of the drug was acceptable.

STABILITY STUDIES
The results of stability studies of the hard gelatin capsules showed in the table. Indicated significant changes in tablet and hard gelatin capsules formulation with time. The stability of the capsules was acceptable.

CONCLUSION
The study was under taken with an aim to formulate, develop and evaluate the Solid dispersed granules of Telmisartan 100mg in hard gelatin capsules. Preformulation study of Telmisartan was done initially and results directed further course of formulation. Based on preformulation studies different batches of Telmisartan were prepared using selected polymers. The prepared drug was evaluated for identification appearance and drug content, before being capsulated has hard gelatin capsules. Hard gelatin capsules tested for weight variation, disintegration and content uniformity as per official procedure. Dissolution of hard gelatin capsules are prepared F1 batch was carried out in 0.1 N HCl media and percentage drug release profile shows 95.4% was satisfactorily performed.

Based on stability testing of hard gelatin capsules, it was concluded that Telmisartan capsules were stable satisfactorily. From the above results and discussion it is concluded that formulation of Telmisartan capsule F1 can be taken as an ideal or optimized formulation. Our study encourages further clinical trials on this formulation.

REFERENCES