In conclusion, sustained release two layered suppositories (STLS), prepared in this study, could be a very useful dosage form for the treatment of asthma, particularly for nocturnal attack. Drug coat L100 and drug coat S100 could be good substitutes for eudragit which is widely used as a drug retarding agent.

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Development of Dissoulution Medium for Rifampicin Sustained Release Formulations

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Dissolution of drugs from solid dosage forms is a key parameter during the product development, formulation and through out the product storage. Rifampicin is very stable in the solid state. Rifampicin transforms into rifampin quinone in mildly alkaline solutions and in presence of atmospheric oxygen at room temperature. The main decomposition product of rifampicin in aqueous acidic medium was 3-formyl rifampicin SV. The decomposition of rifampicin in aqueous solution is diminished by the addition of reducing agents such as ascorbic acid and sodium ascorbate. In USP, 0.1 N HCl is an official dissolution medium and the amount of rifampicin was estimated in comparison with a standard solution having a known concentration of rifampicin concomitantly held at the same temperature for the time specified. This is not suitable for studying release kinetics of controlled release formulations. For this reason, stability of rifampicin in different aqueous fluids and buffers of varying pH in the presence of ascorbic acid as reducing agent was studied. The results indicated that rifampicin was more stable in phosphate buffer of pH 7.4 containing 0.02% w/v of ascorbic acid. Drug release studies of commercial products were done by using this medium and they were compared with the official USP method. This medium was found to be more suitable for studying rifampicin controlled release formulations.

Dissolution of drugs from solid dosage form is an important parameter in assessing the release rate, its mechanism and kinetics during product development. It is also essential for ensuring the product content and uniformity at the formulation stage as well as during its storage. It is important to accept any method of analysis that the analysate is not affected during analysis. For drugs such as rifampicin in aqueous solution, either acidic

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or basic pH range is unsuitable due to presence of atmospheric oxygen. Becuase of the known instability of rifampicin, Gharbo *et al*[1]. studied the percent decomposition of rifampicin in various solutions using high pressure liquid chromatography. They found that rifampicin decomposes by 13% in 1 h and by 29% in 2 h in 0.01 N HCl at 37°, but only by 1% and 2% in water at 37°. In 0.1 N HC1, 17% of rifampicin was degraded in 45 min 37% in 2 h at 37° and 6% and 12%, respectively, in simulated gastric fluid. These authors reported a dissolution medium, consisting of 0.4% sodium laury1 sulfate in water, which would not cause any degradation of rifampicin upto 2 h.

In the USP, 0.1 N HC1 (pH 1.2) was reported as a dissolution medium for rifampicin capsules. For determining the quantity of released rifampicin, a known concentration of standard solution calculated on the dry basis was taken in the same medium prepared concomitantly and held at the same temperature in a water bath for 45 min time. This is a cumbersome process and is not suitable for studying dissolution profiles of controlled release formulations due to decomposition of rifampicin. It was reported[2] that the stability was maximum at pH 5.0 and also the oxidation can be prevented by the addition of sodium ascorbated or ascorbic acid to the solution. Hence, it was decided to study the solubility and stability of rifampicin in presence of ascorbic acid in various aqueous media with an objective to develop a suitable dissolution medium, which can be used to study the release profiles of rifampicin.

Rifampicin IP was obtained from Aristo Pharmaceuticals Ltd., Madhya Pradesh. Potassium dihydrogen orthophospahte was procured from Qualigens Fine Chemicals, sodium hydroxide, hydrochloric acid and ascorbic acid of analytical grade were procured from S.D. Fine Chem., Ltd. Two marketed products of rifampicin capsules (RCIN 300, Batch No. 7001, Mfg. Jan. 97, Lupin laboratories LTd and RIFAMINAL, Batch No. 3253, Mfg. Mar. 97, Alembic Chemical Workds Co. Ltd.) were used in the present investigation.

Accurately weighed quantities of rifampicin were dissolved separately in 100 ml each of 0.1 N HCl and pH 7.4 phosphate buffer. Hundred millilitres of drug solution in 0.1N HCl was divided equally in two volumetric flasks. Like - wise the phosphate buffer solution was divided in another two volumetric flasks equally so that each volumetric flask contained 50 ml drug solution. Ascorbic acid (10 mg) was added to one volumetric flask out of the two (200 µg/ml). Two millilitre aliquots from each volumetric flask were taken, diluted to 10 ml (theoretically 60 µg/ml of rifampicin) and absorbance of each was observed at

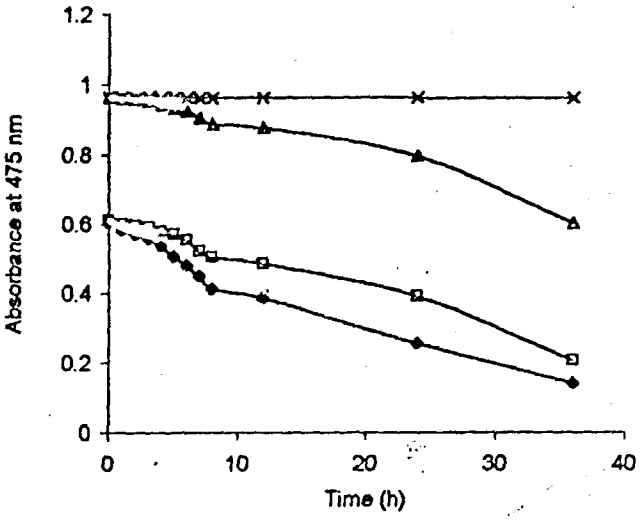

Fig. 1: Stability studies of rifampicin solution

Stability of rifampicin was determined in 0.1N HCl (-◇-) 0.1 N HCl containing 0.02% w/v ascorbic acid (-□-), phosphate buffer pH 7.4 (-∇-) and phosphate buffer, pH 7.4 containing 0.02% w/v ascorbic acid (-x-) Each point is a mean of three determinations

475 nm. The stability of rifampicin was studied for a period of 36 h. Results were shown in fig. 1.

The dissolution rate of pure rifampicin and its release from formulations were studied at 37° in 900 ml of pH 7.4 phosphate buffer containing 0.02% w/v ascorbic acid using a USP apparatus 1 (basket method). The basket was allowed to rotate at 100 rpm. Samples were withdrawn at regular time intervals. The volume withdrawn was replaced with an equal volume of fresh dissolution medium. The samples were suitably diluted and rifampicin content was assayed by measuring absorbance at 475 nm using a Shimadzu double beam spectrophotometer (model-UV 150-02).

Solubility plays a major role in dissolution of a drug substance from a solid dosage form. Correlation between solubility and intrinsic dissolution rate of different drug substances in various media have been well established[3,4]. The maximum solubility of rifampicin in 0.1 N HCl at 37° was 200 mg/ml and in pH 7.4 phosphate buffer at 37° was 9.9 mg/ml[5].

The results shown in the fig.1 indicated that in 0.1 N HCl, degradation starts rapidly from the begining. Addition of ascorbic acid does not prevent degradition in acidic medium. Unlike in 0.1 N HCl, in phosphate buffer of pH 7.4, degradition started slowly. This was prevented by the addtion of ascorbic acid (200 µg/ml) and the drug is stable for more than 24 h. Basing on these results phosphate buffer pH 7.4 containing 0.02% w/v of ascorbic acid was selected and dissolution studies were carried out.

The dissolution rate of pure bulk drug and marketed products were studied by the developed dissolution medium. The amount of rifampicin dissolved from pure drug, marketed product A and marketed product B are 88.8±0.11, 74.01±0.58 and 78.6±0.23%, respectively. The results indicated that the dissolution rates were within the USP[6] limits (not less than 75% (Q) of the labelled amount of $C_{43}H_{58}N_4O_{12}$ is dissolved in 45 min).

In conclusion, a dissolution medium of pH 7.4 phosphate buffer containing 0.02% w/v ascorbic acid was found to be most suitable for studying the release profiles of rifampicin from rifampicin sustained release formulation without significant degradition.

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Spectrophotometric Methods for the Determination of Chlorzoxazone in Tablets

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Three simple and sensitive spectrophotometric methods (A-C) in visible region have been developed for the determination of chlorzoxazone. The reactions in all the three methods (A-C) are stoichiometric oxidations when the drug is treated with an excess of oxidant [nitrous acid (HNO_2), method A; N-bromosuccinimide (NBS), method B; chloramine T (CAT), method C] in acidic medium. The unreacted oxidant is then estimated colorimetrically by using an oxidisable dye [cresyl fast violet acetate CFVA), method A; celestine blue (CB), method B; Gallocyanine (GC), method C]. Beer's law limits for methods A, B and C are 0.4 – 4.0 µg/ml, 0.4 – 5.0 µg/ml and 2-12 µg/ml respectively. No interference was observed from tableting additives and the applicability of the methods was examined by analyzing tablets containing chlorzoxazone.

Chlorzoxazone (CZZ) is a central muscle relaxant employed in the treatment of painful musculo skeletal conditions. The existing analytical procedures reported for its determination are based mainly on either HPLC[1-7] or UV spectrophotometry[7-18], while other methods include GLC[16-18] and titrimetry[19,20]. The only reported visible

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