Chapter 5.4
Drug degradation study from fixed dose combination of Rifampicin and Isoniazid

5.4.1. Analytical methods

Gradient HPLC method was used for simultaneous determination of rifampicin (RIF), isoniazid (INH) and 3-Formyl rifamycin (3-FRSV) as discussed in chapter 5.1.2.3.

5.4.2. *In vitro* drug degradation from novel dosage form

The final fixed dosage form was made by placing one RIF 150 mg SR tablet and one INH 75 mg enteric coated SR tablet or INH 75 mg equivalent enteric coated SR pellets together in size 00 capsule. Fig.1 portrays RIF and INH fixed dose combination final formulation schematic diagram.

The *in vitro* drug degradation study was performed using United States Pharmacopeia (USP) 30 type II apparatus at 50 rpm (VDA 6-DR, Veego Instruments Corporation, Mumbai, India) using 900 ml, 0.1N HCl as dissolution media for 2 hours at 37±0.5^{o}C. The formation of 3-FRSV was measured at the end of 2 hour by withdrawing and analyzing the sample by above analytical method. The INH tablet for carefully taken out at the end of 2 hour and transferred to other vessel for carrying out dissolution in pH 6.8 phosphate buffer wherever further analysis require.

For comparison of 3-FRSV formation from plain drug and developed RIF formulation, dissolution studies was carried out in 0.1N HCL using USP apparatus-II, 900 ml media 50 rpm rotation and 37±0.5^{o}C temperature for upto 2 hours for plain drug and upto 8 hours for floating SR dosage form.

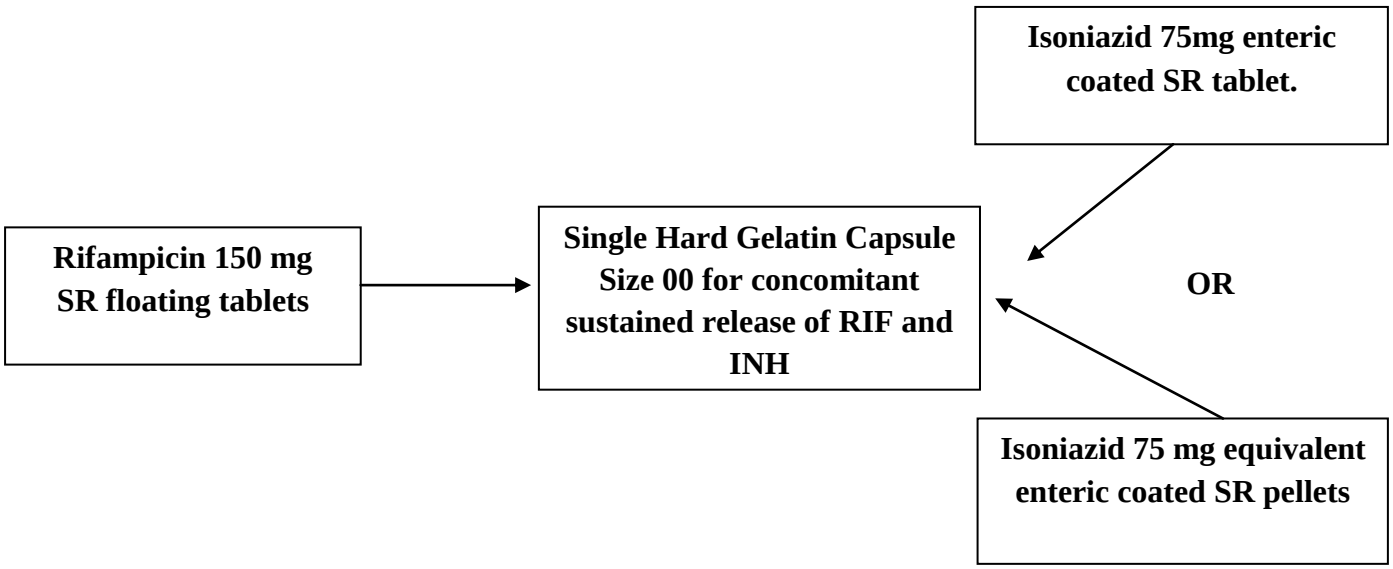

Fig. 1: Schematic diagram of RIF and INH fixed dose combination

Shishoo *et. al.* reported that around 12% of RIF degraded to 3FRSV in acidic medium in 45 minutes from 150 mg dose of RIF [1] and Gohel and Sarvaiya reported 22% of 3FRSV formation in acidic medium from 300 mg dose of RIF in 75 minutes [2].

On the while Shishoo *et. al.* reported around 21% of RIF degradation in 45 minutes when a RIF release study was performed in the presence of INH. Furthermore, Singh *et. al.* reported that 17% to 24% of RIF degradation in 0.1 N HCl at 37^{o}C in 50 minutes when RIF was released with INH [3].

The results of *in vitro* degradation study of developed novel extended release dosage forms are represented in Table 1.

Table 1: *In vitro* degradation study of RIF

Formulation	Percentage of RIF degraded to 3-FRSV
RIF powder 150 mg	11.12%
RIF developed floating sustained release tablet 150 mg	6.53%
RIF developed floating sustained release tablet 150 mg+ INH enteric coated sustained release tablet 75mg	6.95%
RIF developed floating sustained release tablet 150 mg + INH enteric coated sustained release pellets 75 mg	6.65%

From Table 1 it can be concluded that degradation was minimized to great extent from developed novel extended release formulation. This diminish degradation could be due to sustained release of RIF in the acidic medium and segregating RIF and INH zones of drug release and delivery. The results of the research envisaged reveal the effectiveness of novel dosage form segregating drug delivery of RIF and INH and thereby reducing the degradation of RIF in presence of INH. Thus, delivering INH in the intestine and its enteric coating is justified.

5.4.3. References

1. Shishoo, C.J., Shah, S.A., Rathod, I.S., Savale, S.S., Kotecha, J.S., Shah, P.B., 1999. Stability of rifampicin in dissolution medium in presence of isoniazid. Int. J. Pharm. 190(1), 109-123.
2. Gohel, M.C., Sarvaiya, K.G., 2007. A novel solid dosage form of rifampicin and isoniazid with improved functionality. AAPS PharmSciTech 8, E1–E7.
3. Singh, S., Mariappan, T.T., Sharda, N., Kumar, S., Chakrabarti, A.K., 2000. The reason for an increase in decomposition of rifampicin in the presence of isoniazid under acid conditions. Pharm. Pharmacol. Commun. 6,405-410.