Extended Release Metformin HCl-hydroxypropyl Cellulose and Hydroxypropyl Methylcellulose Matrix Tablets and Influence of Additives on the Drug Release Kinetics and Mechanism

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Purpose
To design extended release matrix tablets of metformin HCl using hydroxypropyl cellulose (HPC-H Nisso) and hydroxypropyl methylcellulose (HPMC-K100M) and evaluate the effect of soluble and insoluble additives on the drug release mechanism.

Methods
HPC and HPMC compacts were prepared at drug:polymer ratios of 2:1 and 3:3:1, lubricated with 1% Pruv, by water/IPA granulation and direct-compression methods respectively, using compaction machine at 3500 psi. Soluble or insoluble additives were included at 10 or 18.6% in HPC or HPMC compacts respectively. Dissolution studies (Distek) were performed in 1000mL pH 6.8 buffer at 100rpm; assaying drug at 235nm.

Results
Optimization indicated an extended metformin HCl release profile over 11h at drug:polymer ratio of 2:1 and 3:3:1 for HPC and HPMC respectively. Fig 1 depicts % drug released vs. time data fitted by $C = C_0e^{-kt}$, $k = 1$st order rate constant. In the case of IPA granulated compact, adsorbed IPA on the granules, allowing quick hydration of HPC forming a barrier, possibly retarded drug dissolution rate. Soluble additives increased and insoluble additives decreased the drug release rate. Soluble povidone with gelatinous mass decreased the rate plausibly by blocking channels in cellulosic polymer diffusion pathway (Patel N. et al. Int.J.Pharm.318,15,2006). Soluble SLS decreased the rate possibly by forming micellar aggregates in the channels plus its wetting property. In power law $M(t)/M(\text{Infinite})=kt^n$, exponent $n$ is predictive of drug transport mechanism through polymeric matrix (Rinaki. Int.J,Pharm. 255,199,2003). Fig 2 illustrates $ln f$, fraction metformin HCl released vs. $ln t$ and the data were fitted using linear least square method to obtain straight lines. $n$ value decreased in presence of insoluble additives reflecting change in drug release mechanism from anomalous transport toward Fickian diffusion.

Conclusion
Metformin HCl-HPC and -HPMC matrix tablets at drug:polymer ratio of 2:1 and 3:3:1 yielded extended release profile. The additives at 10% (HPC) and 18.6% (HPMC) can modulate the drug release. The $n$ values from the power law inferred that additives altered the drug mechanism from anomalous transport towards Fickian diffusion by physical state of the additives in diffusion pathway.