11 Summary

Salbutamol sulphate and theophylline both the drugs are widely used in asthma and related disease. It works by relaxing the smooth muscle cells of bronchi. Salbutamol sulphate is a moderately selective beta (2) receptor agonist similar in structure to terbutaline and theophylline, an xanthine derivative chemically similar to caffeine and theobromine. Dual retard tablets of salbutamol sulphate and theophylline were prepared in such a way that salbutamol sulphate released quickly to produce the quick action and theophylline was released in sustained action for 12 hr. By preparing dual retard tablet formulation of salbutamol sulphate and theophylline, reduces the frequency of dose, gives maximum bioavailability, reduces the side effects and maintain the drug serum concentration in the therapeutic window. By developing dual retard tablet, patient compliance can be increased as b.i.d. dosage form.

Dual retard tablet production requires two major parts i.e. immediate release part and sustained release part. In our work, salbutamol sulphate was embedded in immediate release part and theophylline was embedded in sustain release part. To optimize the formula for salbutamol sulphate IR is very important step. Microcrystalline cellulose was considered as filler and the concentration of 20% w/w of MCCP was kept constant in all batches. In this optimized filler batch, various super disintegrating agents like Sodium starch glycolate (SSG), Cross carmellose sodium (CCS), pregelatinised starch and kyron T-314 were used with their optimum prescribed concentration. Once again the batches were evaluated for flow property as well as pharmaco technical parameters including in-vitro dissolution. By evaluating various parameters, the batch containing kyron T-314 (6%) released the drug within 10 min and found to be the best amongst other super disintegrating agents.

So, as an immediate release part, the formulation containing kyron T-314 (6%) with MCCP as a filler was considered to be used in dual retard tablet.

Now another major part was to formulate and optimize the theophylline sustain release formulation. After referring many articles, it was concluded that theophylline sustain release can be formulated by hydrophilic polymer (HPMC) as well as hydrophobic polymers (ethyl cellulose and eudragit RSPO). All the batches were formulated by non aqueous wet granulation method. All the batches were evaluated for flow property and pharmaco technical parameters. Some of the concentration of polymers was not suitable as they retard the drug for more than 12 hr or less than 12 hr. But below mentioned five conc. of different polymers were able to remain sustain for 12 hr. i.e. HPMC K4M (20%), HPMC K15M (15%), HPMC K100M (10%), ethyl cellulose (10%) and eudragit RSPO (20%). The flow property of all
the batches was good. By applying the data to mathematical kinetic models, all of five formulations followed zero order drug release by diffusion mechanism. After considering evaluation data and cost factor, following three formulations were considered to manufacture dual retard tablet i.e. HPMC K100M (10 %), ethyl cellulose (10 %) and eudragit RSPO (20 %)

Three batches of dual retard tablet were prepared by using optimized batch of salbutamol sulphate immediate release part kyron T-314 (6 %) with MCCP and above mentioned three different formulation of theophylline sustained release part. In-vitro study revealed that only batch D1 released salbutamol sulphate in 60 min. The other two batches of dual retard tablet took 2 hr to release salbutamol sulphate. All the formulation of dual retard tablet released theophylline in 12 hr. Flow property of all the three batches was good. All the formulation of dual retard tablet followed zero order drug release kinetic by diffusion mechanism. The optimized batch D1 was also checked for interference by FTIR spectrograms. Accelerated stability study was also done for one month and found therapeutic stable. So, batch D1 was consider as the best formula to prepare dual retard tablet of salbutamol sulphate and theophylline which gives quick onset of action as well as for longer time duration.

The other study deals with formulation, optimization and evaluation of dual retard floating tablet of amlodipine besylate and atenolol. Immediate release part contains amlodipine besylate required for onset of action and sustain release part contain atenolol required for extend the action of drug. Preformulation study was carried out for measurement of drug micromeritic property and drug-excipients compatibility study. Drug-excipients compatibility study was shown that there was no interaction between drug and excipients. The superdisintegrand kyron T-314 was selected for immediate release part. amlodipine besylate was released within 30 min which provide quick onset of action. The polymers hydroxypropyl methyl cellulose and xanthan gum were used as release rate controlling polymers by forming matrix gel like structure and combination of sodium bicarbonate and citric acid was used as gas generating agent. Optimization for atenolol sustain release layer was done using $3^2$ full factorial designs. The controlled release of atenolol was observed for 12 hr and zero order release profile was followed in optimized batch. Stability study of bi-layer tablet showed that there was no major effect of temperature and relative humidity on assay and in-vitro drug release profile which indicated that dual retard floating tablet of amlodipine besylate and atenolol is stable formulation.
Thus, an attempt was made to design an effective, stable formulation was feasible with the advantages of sustain release and immediate release action with a minimum amount of dose for asthmatic as well as antihypertensive patients.

Experience with dual retard tablet reveals that this is a fruitful approach to prepare dual retard tablet for better action (immediate as well as sustain) of combination of salbutamol sulphate with theophylline and amlodipine besylate with atenolol.