Poster Session 1 – Biopharmaceutics

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Impact of formulation variables on the in vitro release profiles of furosemide gastric floating drug delivery system

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It was proposed to investigate the effect of formulation composition (amount of HPMC, sodium bicarbonate and alginic acid) on in vitro drug release and floating properties of a poorly water-soluble drug (furosemide). Matrix tablets were prepared by direct compression using a 10-station tablet machine (Rimek Mini Press-I, India; Table 1). In vitro dissolution studies were performed in 900 mL of phosphate buffer (pH 5.8, 37 ± 0.5, 100 ± 2 rev min^{-1}) using USP apparatus-I (GMP model, Electrolab, TDT-08L, India). The Korsmeyer & Peppas (Peppas 1985) equation was used to compare the drug release kinetics and mechanism from matrix tablets. In vitro floating properties were observed by placing tablets in 200 mL of 0.1 M HCl and lag time, and the axial and radial swelling of tablets were determined after 8 h of floating study. In vitro dissolution data showed that release characteristics were dependent on the amount of HPMC with drug release decreasing with increasing polymer concentration. As polymer concentration increases there is a corresponding increase in gel layer thickness with a decreased tendency of solvent penetration into the matrix and decreased drug release. Sodium alginate does not appear to offer any delay in drug release when formulated with higher viscosity grade HPMC at the concentrations tested. Sodium bicarbonate had an appreciable effect on in vitro release of furosemide with increasing concentration increasing release rate. As sodium bicarbonate effervesces following contact with the dissolution medium, the resultant pores create additional access channels for dissolution media within the tablet matrix. A correlation between HPMC, sodium bicarbonate and sodium alginate content and release rate ($R^2 = 0.83$–0.954), and Korsmeyer Peppas variables (K and n values). Most of the formulations showed excellent in vitro floating characteristics for more than 7 h with lag times of less than 10 min and appreciable radial (> 50%) and axial (> 100%) swelling after 8 h of study. In conclusion, formulation compositions of matrix tablets had a significant effect on in vitro performance.

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Table 1 Formulation composition and performance of matrix tablets

Formulation					Release analysis	
Code	Fu mg	SA mg	SB mg	HPMC mg	n	K (h^{-n})
F1	40	5	10	60	0.40 ± 0.07	0.14 ± 0.04
F2	40	5	10	70	0.41 ± 0.02	0.25 ± 0.02
F3	40	5	10	80	0.56 ± 0.05	0.19 ± 0.03
F4	40	5	10	90	0.63 ± 0.04	0.15 ± 0.01
F5	40	5	10	100	0.67 ± 0.04	0.13 ± 0.00
F6	40	5	0	70	0.65 ± 0.05	0.06 ± 0.01
F7	40	5	5	70	0.64 ± 0.03	0.12 ± 0.01
F8	40	5	15	70	0.39 ± 0.04	0.39 ± 0.05
F9	40	5	20	70	0.37 ± 0.03	0.45 ± 0.05
F10	40	0	10	70	0.60 ± 0.06	0.24 ± 0.04
F11	40	10	10	70	0.73 ± 0.03	0.15 ± 0.06
F12	40	20	10	70	0.78 ± 0.04	0.13 ± 0.01

Formulation: Fu, furosemide; SA, sodium alginate; SB, sodium bicarbonate; HPMC, HPMC K4 M; Xanthan gum (3 mg). In addition the following excipients were used in all formulations: magnesium stearate (5 mg), purified talc (2 mg), cross-linked PVP (55 mg), lactose fast flow (10 mg).

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Ibuprofen dissolution from solid dispersions

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Solid dispersions can be used to improve dissolution of poorly water-soluble drugs such as ibuprofen (Chiou & Riegelman 1971). Polyvinylpyrrolidone (PVP) and polyethylene glycol (PEG) are common polymeric carriers in such systems. The mechanisms underpinning the observed improvements in dissolution rate are not fully understood and rely on an understanding of the dissolution behaviour of both components of the solid dispersion. In this study, the dissolution of ibuprofen and polymers (PVP-40 and PEG-8000) were investigated using UV spectroscopy and microviscometry, respectively. The ibuprofen:PVP-40 solid dispersions, at a ratio of 1:2, were prepared using spray drying of an ethanolic solution. The ibuprofen:PEG8000 solid dispersions at a ratio of 1:2 were prepared using the co-melting method. Dissolution was carried out in phosphate buffer (pH 6.8) using a standard USP II dissolution apparatus. Microviscometry was used to study polymer dissolution. It measures small changes in the viscosity of the medium as the polymer dissolves from the solid dispersion. Standard polymer solutions were prepared in phosphate buffer (pH 6.8) and measured using microviscometry (Esnaashari et al 2005). Calibration curves were plotted and were found to be linear over the concentration range in these experiments. The viscosity of the dissolution medium containing ibuprofen was found not to differ from the buffer control. Ibuprofen dissolution was found to be greatly enhanced by the formation of a solid dispersion compared with the pure drug (Table 1). Only 8% of the ibuprofen dissolved at 5 min and 47% at 30 min. From solid dispersions, 30% and 43% of the drug dissolved at 5 min and 100% and 83% dissolved at 60 min from PVP-40 and PEG8000, respectively (Table 1). For PVP, dissolution of ibuprofen has been shown to follow the dissolution of the polymer, therefore, it can be suggested that polymer dissolution governs the drug dissolution from the solid dispersion (Esnaashari et al 2005). However, dissolution of PEG8000 was faster than ibuprofen from the dispersion. The mechanisms underlying this improvement in dissolution are yet to be fully elucidated. Different mechanisms may dominate in different solid dispersion systems and from different drug/polymer ratios. Improved wettability, local solubilisation and particle size reduction have been argued to impart the improvement in dissolution from low molecular weight PVP and from PEG solid dispersions. The use of microviscometry offers an easy technique to study polymer dissolution in drug-release studies. Further work is to be undertaken to characterise the solid dispersions and elucidate the mechanisms governing ibuprofen release from PVP and PEG solid dispersions.

Table 1 Dissolution of ibuprofen (IB) and polymers from solid dispersions

	% Dissolved 5 min	30 min
Pure IB	8	47
IB from PVP-40 solid disp	30	100
IB from PEG8000 solid disp	43	83
PVP from solid disp	42	73
PEG from solid disp	93	99

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Esnaashari, S. et al (2005) *Int. J. Pharm.* **292**: 227–230

Poster Session 1 – Pharmacognosy

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Essential oil composition and antibacterial activity of *Stachys acerosa* Boiss

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Stachys acerosa Boiss. (Lamiaceae) is an endemic plant of Iran. Other species of *Stachys*, such as *S. lavandulifolia*, have been used for gastrointestinal and female hormonal disorders in Iranian traditional medicine. In this investigation, essential oils composition and antibacterial activity of the flowering and non flowering tops of *S. acerosa* were studied. The plant materials (flowering and non flowering tops) were subjected to hydro distillation using Clevenger-type apparatus. Essential oils were analysed by GC-MS. Identification of compounds was based on a comparison of their mass spectra with standards. Confirmations of compound identities were achieved by their retention indices (Kovats 1958; Adams 2001). Bioautography method (Vanden Berghe & Vlietinck 1991) was used to screen for antibacterial activity on silica gel GF254 TLC plates with toluene–ethyl acetate (93:7) as mobile phase (Wagner & Bladt 1996), on six standard strains: *Staphylococcus aurous, S. epidermidis, E. coli, Klebsiella pneumonia, Bacillus subtilis* and *Pseudomonas aeroginos*. Essential oils yielded 0.10%