increase in H2AX phosphorylation would indicate that a greater degree of damage is being caused to TamR cells. While one explanation may be that the different effect might be caused by a difference in uptake/efflux of drugs, the fact that this effect is peculiar to bleomycin, etoposide and doxorubicin and not other cytotoxics would suggest that the difference between these two cell lines may lie in their ability to detect and repair DSBs and not in their ability to efflux or metabolise them. Further work will establish the DNA repair capacity of these cell lines, as well as their tendency to commit to apoptosis when subjected to certain stresses in order to better understand the underlying differences that cause this phenomenon of double strand break sensitivity.

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Poster Session 1 – Materials Science

025
Nanoparticle based ciprofloxacin coating formulation for biomedical application

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One of the solutions to overcome medical device related infection is the use of biodegradable coating incorporated with antimicrobial agent. As most drugs have poor solubility in water, coating formulations are derived by using appropriate solvents. However, these solvents have toxicity issues and the use of ethanol or acetone as solvents is generally more acceptable. Preliminary results with these solvents showed that coating solutions with the selected drug candidate, ciprofloxacin, was inhomogeneous and cloudy. An interesting alternative to this situation is formation of a nano suspension of drug particle in ethanol, acetone, or a mixture of the two. In this work, the preparation of ciprofloxacin nano suspension in acetone is reported. This mixture was used to cast film by evaporation. Coating composition with varying concentration of ciprofloxacin (1, 2 and 3% w/w of copolymer concentration) was prepared by dissolving styrene-maleic anhydride (S-MA) copolymer in acetone. The nano suspension (100 nm) of ciprofloxacin was obtained by simultaneously adding an appropriate amount of non-ionic surfactant, Hyoxide AAO (1% w/v). The films were prepared by applying the resulting mixture on a Teflon panel and drying at room temperature for 24 h. Table 1 shows the coating composition and film properties. Film degradation and ciprofloxacin release were studied by placing 1 square inch of film in 100 mL of simulated gastric fluid (pH 1.2) in a stoppered flask in a rotary shaker (37°C, 100 osc. min^{-1}). The amount of ciprofloxacin released as a function of time was determined using a spectrophotometer at 430 nm. Table 1 shows the degradation characteristics and ciprofloxacin released after 10 days. Increasing the amount of ciprofloxacin in the film significantly increased the degradation and thereby the percentage of drug released. Thus, the release of ciprofloxacin coupled with degradation properties of the film indicated its potential as a medical device coating.

Table 1 Coating composition and film properties

No.	S-MA (% w/v)	Drug (% w/w)	% Elongation	% Weight loss	% Release
SMA0	10	0.0	2.23	35	—
SMA1	10	0.1	2.12	11	43
SMA2	10	0.2	2.04	15	58
SMA3	10	0.3	1.97	21	69

Note: Suspension based on total of 100 mL acetone and 1% w/v of non-ionic surfactant.

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026
In-line techniques for end-point determination in large scale high shear wet granulation

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High shear wet granulation is a size enlargement process whereby powders are converted to larger granules through addition of liquid and under mechanical agitation. Despite its widespread use in the pharmaceutical industry, wet granulation has traditionally been considered an empirical art, although in recent years there have been rapid advances in understanding the fundamental processes involved (Lister 2003). In this work three in-line techniques – Power Consumption, Focused Beam Reflectance Measurement (FBRM) and Acoustic Emission – were evaluated for their ability to monitor the wet granulation of a calcium-phosphate-based formulation, particularly focussing on granulation end-point determination. An experimental matrix was designed, varying each of three processing parameters (water added, impeller speed, granulation duration) at three levels to ascertain the extent to which these techniques could differentiate between granulations producing material of different physical properties. All granulations were performed at 50 kg scale in a high shear bottom-driven granulator (PMA200, GEA). Power consumption, a measure of the torque exerted on the impeller by the granulating mass, was found capable of differentiating between different impeller speeds and quantity of water added. However, it was also found that the power curves tended to reach a maximum and then plateau, despite the continued densification of the granules over time. To improve the correlation with granulation behaviour, power consumption data were integrated to give a measure of the total work done during granulation, and this was found to provide an improved relationship with the extent of granulation. FBRM (Lasentec, Mettler-Toledo Autochem) relies on the emission of a laser from a stainless steel probe placed within the granulator to determine particle size during granulation. It was found that upon addition of water to the dry powder, the fine particle counts ($< 100\,\mu$m) were seen to decrease, accompanied by a sharp increase in the 100–1000 μm range and the median particle size. Particle size changes were also observed with the activation of the chopper, showing a decrease in the coarse particle counts. Furthermore, in-line real time FBRM data could follow median granule size growth with increased water added, impeller speed and granulating time, thus offering a potential to aid process control. Probe fouling was not found to be a significant issue with this formulation due to it largely comprising an inorganic filler. Acoustic Emission was used to monitor the intensity of the acoustic profile in the range of 20 kHz to 1 MHz during granulation. The data collected showed a relatively flat profile during the dry mixing phase, followed by a large peak corresponding with water addition, before returning to baseline. This technique offers the potential to develop a fundamental understanding of the interaction of liquid and the dry mass in the early stages of granulation. Further analysis of specific frequency ranges may yield trends in the data that can help with the identification of granulation end-point (Whitaker et al 2000). This work has outlined three in-line techniques that offer the potential to monitor real time physical changes in the granulation process and thereby improve process understanding.

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027
Study of hydrated sugar lyophiles by low-frequency dielectric spectroscopy

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Lyophilisation is commonly used to prepare stable parenteral formulations from compounds with poor inherent solution stability. The stability of these lyophilised systems depends, in part, on their residual moisture following lyophilisation and their propensity to absorb water during storage. Sugars, such as sucrose, are often used as pharmaceutical excipients in such lyophilised systems. The formation of a nearly dry amorphous sugar 'matrix' can help protect the drug from both chemical and physical degradation during storage. Freeze-dried sugars have a porous structure with a very large surface area. Previous studies of non-pharmaceutical porous materials (porous glasses) have shown that the absorbed water molecules in such systems (Gutina et al 2003) form different populations. However, no such studies have been performed for pharmaceutical excipients, and yet new information about the behaviour of water molecules in amorphous sugar matrices could help in understanding drug stability in such systems, and thus facilitate more rationale formulation design. The aim of this work was to undertake a dielectric relaxation study of molecular dynamics in a model freeze-

dried system of partially-hydrated sugars. Three types of sugar (sucrose, lactose and trehalose) were measured by dielectric spectroscopy. Freeze dried powders were prepared from 10% aqueous sugar solutions using a standard procedure. Samples with different moisture content were prepared by re-hydrating from atmospheric moisture under controlled conditions. Dielectric measurements were performed using Solartron 1296 dielectric interface connected to a Solartron 1255 frequency response analyser. The frequency and temperature ranges investigated were 0.1–1 MHz and −120°C to 60°C, respectively. Analysis of the complex dielectric permittivity spectra reveals three relaxation processes, for each type of sugar. All these processes can be associated with the relaxation behaviour of water molecules adsorbed onto the surface of the porous sugar matrix. The first relaxation process (at low temperature) is ascribed to the reorientation of water molecules in ice-like structures comprising either parallel or anti-parallel arrangements of dipoles (depending on temperature). The second process is thought to be due to a single water molecule reorientation in the vicinity of a defect. The third process is observed at low frequency and at higher temperatures (> 0°C) and is due to the self-diffusion of charge carriers through the porous network. These charge carriers are most probably protonic and originate from the water adsorbed on the porous medium. Relaxation parameters for each process were obtained by fitting to the Havriliak-Negami formula (Gutina et al 2003). Comprehensive analysis is presented of the influence of moisture content, temperature and type of sugar on the dielectric parameters extracted from fitting.

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028
Effect of rheology modifiers on tablet disintegration

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To provide better prediction of in vivo performance of a dosage form, thorough assessment of test media is necessary. In recent years, interest has been focused on the development and utilization of physiologically relevant medium components, which attempt to simulate the in vivo conditions of the gastrointestinal tract (e.g., in the body certain natural surfactants aid in the dissolution and subsequent adsorption of drugs with limited aqueous solubility). Thus for enhancing solubility, dissolution medium are being incorporated with surfactants (sodium lauryl sulfate) or hydrophilic polymers (Jones et al 2004). But it is also true that alterations in media composition with such agents would influence factors such as surface tension and viscosity, which in turn will affect tablet disintegration time. The purpose of this study was to examine the disintegration of tablet in media under the influence of rheology modifiers. It was also intended to study whether the rheology modification of medium has a controlling effect on the disintegration time of tablets. Commercially available fast disintegrating antacid tablets were employed to assess the disintegration time in media under the influence of rheology modifiers. Poly (vinyl acetate-co-maleic anhydride), VAMA, was used as a rheology modifier for test medium. VAMA with varying monomer ratio was prepared by precipitation polymerization. The copolymer was characterized by acid value, softening point and molecular weight determination (Raval et al 1997). The surface tension and viscosity of a range of aqueous solutions of VAMA was determined by capillary action method and U tube viscometry, respectively (Fell et al 2005). The disintegration time of tablets was determined using disc as per Indian standard. The results are reported in Table 1. Increasing viscosity and simultaneous decrease in surface tension retards the disintegration time of tablets possibly by reducing the penetration rate of liquid into tablets.

Table 1 Influence of VAMA concentration on tablet disintegration time

Polymer system	Monomer ratio (VA:MA)	Polymer concn (%)	Surface tension (dynes/cc)	Relative viscosity	Disintegration time (s)
VAMA1	1:1.5	1	70.57	1.05	52
		3	65.78	2.56	64
		5	61.64	3.95	69
VAMA3	1:1	1	70.60	2.14	53
		3	68.22	4.43	66
		5	65.84	5.43	76
VAMA5	1:0.5	1	76.28	2.80	55
		3	73.20	8.00	71
		5	69.51	9.85	88

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Poster Session 1 – Pharmaceutical Technology

029
Stomach specific anti-*Helicobacter pylori* therapy: preparation and evaluation of amoxicillin-loaded chitosan mucoadhesive microspheres

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Amoxicillin is widely used for the treating gastric and duodenal ulcers, which are associated with *Helicobacter pylori* (Vakil & Cutler 1999). However, some reports and clinical trials indicate that the therapies cannot bring about compete eradication of *H. pylori* and suggest that the therapeutic effect needs more investigation (Kawabami et al 2001). One probable reason for the incomplete eradication of *H. pylori* is the short residence time of the dosage form in the stomach so that effective antimicrobial concentration cannot be achieved in the gastric mucous layer or epithelial cell surfaces where *H. pylori* exists. Thus, the purpose of this research was to formulate and systemically evaluate in vitro and in vivo performances of mucoadhesive microspheres of amoxicillin. Amoxicillin mucoadhesive microspheres (Amo-mu-ms) containing chitosan as mucoadhesive polymer were prepared by a simple emulsification phase separation technique using glutaraldehyde as a cross-linking agent. Results of preliminary trials indicate that the volume of cross-linking agent, time for cross-linking, polymer-to-drug ratio, and speed of rotation affected characteristics of microspheres. A 3^2 full factorial design was employed to study the effect of independent variables, polymer-to-drug ratio and stirring speed on dependent variables % mucoadhesion, t_{80}, drug entrapment efficiency, particle size and swelling index (Table 1). The best batch exhibited a high drug entrapment efficiency of 70% and a swelling index of 1.39%; mucoadhesion after 1 h was 79%. The drug release was also sustained for more than 12 h. The morphological characteristics of the Amo-mu-ms were studied under SEM. In vitro release test showed that amoxicillin released faster in pH 1.0 hydrochloric acid than in pH 7.8 phosphate buffer. In vitro and in vivo mucoadhesive tests showed that Amo-mu-ms adhered more strongly to the gastric mucous layer and could be retained in the gastrointestinal tract for an extended period of time. In vivo *H. pylori* clearance tests were also carried out by administering Amo-mu-ms and powder, to *H. pylori* infectious Wistar rats under fed conditions at single dose by the oral route. The results showed that Amo-mu-ms had a better clearance effect than amoxicillin powder. In conclusion, the prolonged gastrointestinal residence time and enhanced amoxicillin stability resulting from the Amo-mu-ms might make a contribution to *H. pylori* clearance.

Table 1 3^2 full factorial design layout

Batch no.	Polymer-to-drug ratio	Stirring speed (rpm)	Mucoadhesion after 1 h (%)	t_{80} (min)	Drug entrapment efficiency (%)
S1	1:1	500	53	225	45
S2	1:1	1000	46	223	42
S3	1:1	1500	43	211	38
S4	1:3	500	75	196	65
S5	1:3	1000	67	228	62
S6	1:3	1500	60	241	58
S7	1:6	500	79	465	70
S8	1:6	1000	72	447	68
S9	1:6	1500	64	371	64

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