minimise the need for experimentation and maximise the probability of success of the wet granulation process. This is of particular relevance in the early stages of pharmaceutical development, when formulations are changed frequently. Further work is on-going to develop tools for the quantitative prediction of appropriate fluid levels from first principles.

Table 1 Granulator power end-point for formulations with different sorption potentials granulated at different fluid levels

MCC	CC Na	Sorption potential	Fluid	Power
Low	Low	Low	High	118 W
High	High	High	High	75 W
High	Low	Medium	Low	75 W
Low	High	Medium/High	Low	66 W

Note: MCC and CC Na belong to the (0,1) SLI-classification of low solubility and high sorption potential.

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Application of electrical impedance analysis for investigation of emulsion stabilisers in the frozen state

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The aim of these experiments was to investigate the stability of guar gum-sunflower oil emulsions at below ambient temperatures by examination of impedance response to an applied fixed-frequency electric field while varying temperature, a form of dielectric spectroscopy. Dielectric spectroscopy examines the polarisation-relaxation response of materials when exposed to an electromagnetic field, which is dependent on both structural and molecular properties as well as the ratio of components in mixed systems (Goff 1995). Guar gum is a natural product derived from seeds of the guar plant, *Cyamopsis tetragonolobus*. It is composed of a straight backbone chain of D-mannopyranose units with side branches of D-galactopyranose every other unit. The gum is used as a binding and disintegration component in tabletting in the pharmaceutical industry, as well as a thickener and viscosity promoter in various food products. Analysis was conducted with Lyotherm2 (Biopharma Technology Limited), a thermal analyser capable of assessing impedance during cooling and warming of materials and gives an indication of molecular mobility changes (as a result of events, such as softening, relaxation, crystallisation, rearrangement or melting), which may be applicable to reduced temperature operations for such materials, such as cold storage and freeze drying. Emulsions were prepared by high speed mixing from aqueous solutions of 1.0% m/v guar gum and sunflower oil in three different volumetric ratios: 1:1, 5:1 and 10:1. Cooling to $> 40^{\circ}C$ below the maximum impedance temperature was provided within the liquid nitrogen chamber and the samples were reheated to $0^{\circ}C$ (at $1.5^{\circ}C\,min^{-1}$). The data was exported directly to Microsoft Excel for analysis of the warming profile to determine the temperature of significant events, which may be due to increases in molecular mobility or relaxation. The T_{Zonset} values (onset point of elevated mobility) shown in Table 1 for the 5:1 and 10:1 aqueous:oil emulsions indicate that the system remains immobile until the temperatures rises above $-20^{\circ}C$ (-13.19 and $-15.22^{\circ}C$, respectively). In terms of cold storage, this data indicates that these emulsions could safely be retained in a standard $-20^{\circ}C$ freezer with minimal molecular mobility. Comparing T_{ZL} values (temperature point at which sample begins to deviate from maximum impedance, 5625 kΩ, under an applied field frequency of 1 000 Hz) in Table 1, there is a dramatic decrease in T_{ZL} between the 1:1 and 5:1 emulsions, indicating the enhanced molecular mobility of the latter. The 5:1 and 10:1 emulsions have similar T_{ZL} values (-51.73 and -59.56 kΩ, respectively), indicating that the major difference seen in the system is due to variations in the ratio of aqueous and oil phases (Moran et al 2000). At increased ratios of the aqueous guar phase, impedance is reduced as a function of the conducting properties of water molecules (McCrystal et al 2002). Concurrently decreasing the proportion of oil also leads to a reduction in impedance because the sunflower oil acts to decreases the effective electric field due to enhanced permittivity, thus increasing the capacitance of the system. In conclusion, these results may indicate that the storage of guar gum to minimise molecular mobility (below $0^{\circ}C$), can be achieved at $-20^{\circ}C$. This may have stability advantages for the processing, storage and transport of drug delivery systems incorporating guar.

Table 1 Summary of thermal events accompanying the reduction in impedance values approaching $0^{\circ}C$ three different aqueous 1% m/v guar gum-sunflower oil emulsions (1:1, 5:1, 10:1 v/v)

Sample	Thermal event	Change	Impedance event (°C)
1:1	Melt	T_{ZL}	−2.77
		T_{onset}	−0.50
		T_{end}	−0.40
		T_{Zmelt}	−0.17
5:1	Melt	T_{ZL}	−51.73
		T_{onset}	−13.19
		T_{end}	−11.33
		T_{Zmelt}	−9.04
10:1	Melt	T_{ZL}	−59.56
		T_{onset}	−15.22
		T_{end}	−12.60
		T_{Zmelt}	−9.08

T_{ZL}, temperature point of deviation from the maximum impedance (5625 kΩ) under an applied field of frequency 1000 Hz; T_{onset}, onset point of an elevated mobility region; T_{end}, end temperature point of elevated mobility region and T_{Zmelt}, point of sudden onset of mobility indicating a thermal melting event.

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Poster Session 2 – Biopharmaceutics

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The use of discriminant analysis to identify molecules with potential as enhancers of percutaneous absorption

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Various methods have been used to enhance percutaneous absorption, including the co-formulation of enhancer chemicals, where the enhancer may be the formulation vehicle itself, such as ethanol or propylene glycol, or a chemical dissolved in the vehicle. Such chemicals have been variously termed penetration enhancers, accelerants or sorption promoters. They may be grouped into various chemical categories, such as terpenes, and variations on the Azone (N-dodecylazacycloheptan-2-one) lead molecule. In this study enhancing power (ER) is quantified as the ratio of drug permeated after 24 h relative to control. The standard approach uses regression to yield QSAR equations that predict ER. Discriminant analysis assigns novel compounds to one of a set of groups with a predetermined range of properties and has been successfully applied to the prediction of maximal flux from unenhanced aqueous vehicle (Magnusson et al 2004). We report the success of this approach in predicting whether a novel compound will have an ER value > 10. Data are available for 73 enhancers of hydrocortisone permeation from propylene glycol across hairless mouse skin from the same laboratory. Enhancers had chain lengths (CC) from 0 to 16 carbon atoms, 1 to 8 H-bonding atoms (HB), MW 60 to 450, octanol/water partition coefficients (P) and molar aqueous solubility (S) were calculated. LogP ranged from -1.7 to 9.7 and logS from -7.8 to 0.7. These predictive properties were chosen because of their ready availability. ER values ranged from 0.2 to 25.3. Multiple regression analysis failed to predict activity, with 'good' enhancers (i.e. ER > 10) being underestimated. Simple guidelines suggest that high ER is associated with CC > 12 and HB 2–5. This was refined by multivariate analysis to identify significant predictors. Discriminant analysis using CC,

HB, logP and logS correctly assigned 11 of the 12 'good' enhancers (92%). Twelve of the sixty-one 'poor' enhancers (20%) were incorrectly assigned but 3 could be considered marginal (ER > 8). It is recognised that the methodology has been applied to the enhancement effect on a single drug. The effectiveness of an enhancer may vary with the physico-chemical properties of the drug as measured by its logP value, and the state of thinking regarding the enhancement of percutaneous absorption has recently been reviewed (Williams & Barry 2004). We are currently examining how far our approach can be extended to provide a general prediction of activity. The success of this simple approach in identifying potent enhancers suggests that it is sufficiently reliable to identify potential transdermal enhancers for in vitro screening.

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Poster Session 2 – Pharmacognosy

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Studies on the anti-psoriatic activity of gossypol and its derivatives followed by pre-formulation and formulation studies of gossypol into a topical dosage form

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Gossypol, a natural anti-inflammatory compound, has been studied extensively since the discovery of its in vivo male antifertility activity in the late 1960s and has since shown anti-viral, anti-parasitic and anti-tumour activity. Psoriasis is a multifactorial skin condition characterised by benign keratinocyte hyper-proliferation, skin inflammation, defective keratinisation, altered dermal vasculature and insufficient anti-oxidant activity. In this study the in vitro anti-psoriatic activity of gossypol and its derivatives was evaluated using an anti-proliferative assay and an anti-oxidant assay (Dodou et al 2005). In the anti-proliferative study, the sensitivity of an HPV-16 keratinocyte cell line to each compound was determined using an MTT viability assay. The compounds that showed increased inhibition against keratinocyte proliferation were subsequently tested for their anti-oxidant effect against iron/ascorbate dependent lipid peroxidation, using the thiobarbituric acid (TBA) test. Racemic gossypol ($GI_{50} = 5.4 \pm 0.03\ \mu M$) and its enantiomers were the most potent compounds against the proliferation of HPV-16 keratinocytes, followed by the half-Schiff's bases ($GI_{50} = 15$–$50\ \mu M$), racemic gossypolone ($GI_{50} = 47.3\ \mu M$) and the bis-Schiff's bases ($GI_{50} > 100\ \mu M$). A comparison was made with the data from the MTT assays on HPV-16 keratinocyte cell lines using methotrexate ($GI_{50} = 148\ \mu M$) and dithranol ($GI_{50} = 0.58\ \mu M$). All tested compounds showed similar anti-oxidant activity ($IC_{50} \approx 17\ \mu M$) and were more potent than the positive control propyl gallate ($IC_{70} = 100\ \mu M$). Pre-formulation and formulation studies were then conducted on racemic gossypol, which was the most active compound according to the biological assays. The pre-formulation studies included saturation solubility in hydrophilic and lipophilic vehicles, compatibility with excipients, partition co-efficient over pH range 2–8, and physicochemical stability in solution under extreme light, heat, acidic, basic and oxidising conditions (Dodou 2004). Gossypol showed better solubility in lipophilic vehicles ($> 3\ mg\ mL^{-1}$) than hydrophilic ones ($< 1.5\ mg\ mL^{-1}$) and its water solubility was $0.075\ mg\ mL^{-1}$. It was compatible on storage with commonly used excipients in tetrahydrofuran (THF) solution at 25°C for 6 days. It was found to be stable in acidic, basic and high temperature conditions but was prone to oxidative and photolytic degradation. Its logP value was around 5–6 at pH < 5. The oil in water (o/w) cream of racemic gossypol ($0.065 \pm 0.03\%$ w/w) was physically and chemically stable on storage at temperatures below 30°C for 9 days, had pH = 3.2 and a median oil droplet diameter of $20\ \mu m$. In vitro release studies using Franz diffusion cells and a regenerated cellulose membrane showed that the cumulative flux of gossypol was $6.3\ \mu g\ cm^{-2}$ after 9 h. Gossypol was shown to be the most potent inhibitor of keratinocyte proliferation in the anti-proliferative MTT assay, a potent anti-oxidant in the TBA assay, and its formulation into a topical dosage form was feasible. The above findings, in conjunction with its low human toxicity and lack of mutagenic effects, make gossypol a good candidate for the topical treatment of psoriasis.

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Characteristics of traditional Chinese herbal medicine (TCHM) retail outlets in central London: preliminary results of a cross-sectional study

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In the UK, unlicensed traditional Chinese herbal medicines (TCHMs) are widely available for over-the-counter purchase from TCHM retail outlets without the involvement of a statutorily regulated health care professional. Pharmacovigilance (safety monitoring) for herbal medicines is in the early stages of development (Barnes 2003) yet, in recent years, safety concerns have emerged associated with Chinese herbal remedies prepared by TCHM practitioners and manufactured TCHMs available for purchase from TCHM retail outlets (Barnes et al 2004). These issues raise questions about aspects of TCHM outlets, yet there is a lack of formal study of practices of such shops in the UK. This study aimed at exploring the characteristics of TCHM retail outlets in central London, including types of products sold and medical uses/conditions for which TCHM is promoted. A semi-structured questionnaire, which included questions regarding information visible inside and outside TCHM outlets, was designed and developed, tested for face validity and piloted on five TCHM retail outlets outside the chosen study area. Potential TCHM outlets, including complementary medicine providers, health-food stores and pharmacies, in the study area (W1 postcode) were identified systematically by searching the Yellow Pages on-line directory. After a screening procedure (physically visiting every street in W1), 12/173 (7%) outlets were classified as TCHM retail outlets. A letter describing the study was posted to each outlet one week before the data collection period. Data were collected for the 'outside' of all 12 outlets, and detailed 'inside' observations were done for the four outlets consenting to this. Overall, 11/12 outlets displayed manufactured TCHM products, and nine used drawers or transparent jars to display Chinese crude herbs. Eight of the 12 outlets listed medical uses/conditions visible outside the shop; the median number was 25.5 ($Q_L = 16.25$, $Q_U = 59.5$). There were 274 occurrences of 137 different terms for uses/conditions; each term was counted once only for each shop. Similar terms were combined to produce 108 use/condition categories. Table 1 presents the three most frequently listed categories for the three most common therapeutic areas, after classification by BNF chapter (BMA and RPSGB 2005). Other uses/conditions listed of particular interest include cancer, diabetes, HIV infection and contraception. Also, 77 TCHM-related advertisements were identified within 11 shops; of these, 38 were associated with specific uses/conditions, most commonly skin problems, weight loss and hair loss. TCHM retail outlets in central London sell both crude herbs and manufactured TCHM products. These outlets readily display names of serious medical conditions on their premises, visible to passers-by, which at least implies that TCHMs can be used to prevent, treat or cure these conditions.

Table 1 Most frequently use/condition categories listed

BNF chapter	Use/condition category	n (% of total N; N = 274)
Central nervous system	Stress/Anxiety/Relaxation	10 (3.6%)
	Obesity/Sliming/Weight loss	8 (2.9%)
	Insomnia/Sleeplessness	7 (2.6%)
	Total	53 (19.3%)
Obstetrics, gynaecology and urinary-tract disorders	Infertility	8 (2.9%)
	Menstrual problems	7 (2.6%)
	Impotence	6 (2.2%)
	Total	39 (14.2%)
Skin	Hair Loss	7 (2.6%)
	Eczema	6 (2.2%)
	Psoriasis	6 (2.2%)
	Total	37 (13.5%)

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