percutaneous permeation enhancer. Nevertheless, the results of this investigation indicate a novel means of enhancing absorption of poorly permeable drugs.

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Enhancement of Dissolution Rate of Meloxicam

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Solid dispersions of meloxicam (MX) in polyvinyl pyrrolidone (PVP), hydroxy propyl methyl cellulose (HPMC), hydroxy propyl cellulose (HPC) and polyethylene glycol 6000 (PEG) and solvent deposited systems on lactose, soluble starch, microcrystalline cellulose (MCC), dicalcium phosphate (DCP), silica gel and their selected tablet formulations were investigated with an objective of enhancing the dissolution rate of MX. A marked enhancement in the dissolution rate and dissolution efficiency of MX was observed with all solid dispersions and solvent deposited systems. Among the carriers used in solid dispersions PVP gave highest enhancement (19 fold) in the dissolution rate of MX at 9:1 ratio of drug and carrier and in the case of solvent deposited systems MCC and DCP gave an improvement of 13.1 and 17.5 fold in the dissolution rate of MX respectively at 1:2 ratio of drug and excipient when compared to MX itself.The solid dispersions in PVP and HPMC and the solvent deposited systems on MCC and DCP could be formulated into tablets.These tablets, apart from fulfilling the official and other specifications, exhibited higher rates of dissolution and dissolution efficiency values.

Meloxicam[1] is an effective, new nonsteroidal antiinflammatory and analgesic drug. It is practically insoluble in aqueous fluids and its aqueous solubility was found to be 20 mg/l. The very poor aqueous solubility of the drug gives rise to difficulties in the formulation of dosage forms and may lead to variable dissolution rates

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and bioavailabilities. It is not yet official in any pharmacopoeia. Though a few tablet formulations of meloxicam are available commercially, no work was reported on the pharmaceutical formulation aspects of meloxicam, its dissolution rate and bioavailability. In the present work solid dispersion[2] and solvent deposition[3] techniques were tried to enhance the dissolution rate of meloxicam.

Meloxicam was a gift sample from M/s Sun Pharmaceuticals, Baroda. Polyvinyl pyrrolidone (BASF, PVP K-30), hydroxy propyl methyl cellulose-SL (NISSO, having a viscosity of 3.0-5.9 cp in a 2% by weight aqueous solution at 20°), hydroxy propyl methyl cellulose (Pharmacoat 606; having a viscosity of 6 cp in a 2% by weight aqueous solution at 20°), microcrystalline cellulose (Avicel, FMC, PH 105), Primogel (sodium starch glycollate) were gift samples from M/s Veco Pharma Ltd., Visakhapatnam. Polyethylene glycol 6000 (SD Fine Chem), lactose IP (SD Fine Chem), soluble starch (Loba Chemie), dicalcium phosphate (Loba Chemie), silica gel (SD Fine Chem), acacia (SD Fine Chem), dichloromethane (Qualigens), methanol (Qualigens), talc IP and magnesium stearate IP were procured from local market.

The following commercial formulations of meloxicam were also included in the study for comparison purpose. M-Cam tablets (each containing 7.5 mg of meloxicam), (M/s Unichem Laboratories Ltd., Mumbai, Batch No. MCL 99035, Mfg. Date: 6/99, Exp. Date:5/2002 and Melod tablets (each containing 7.5 mg of meloxicam) M/s Zydus Cadila, Ahmadabad, Batch No. CM 9002, Mfg. Date: 12/99, Exp. Date: 11/2000.

Solid dispersions (SD) of meloxicam were prepared employing polyvinyl pyrrolidone (PVP), hydroxy propyl methyl cellulose (HPMC), hydroxy propyl cellulose (HPC) and polyethylene glycol (PEG) as carriers in the drug and carrier ratios of 19:1 and 9:1. The solid dispersions were prepared by dissolving meloxicam and the carrier in dichloromethane in the case of PVP, HPMC and HPC and in a solvent blend of dichloromethane and methanol (2:1) in the case of PEG to obtain a clear solution. The solvent was removed by evaporation at 40° under reduced pressure (8 in Hg Abs.). The mass obtained was powdered, mixed and stirred through a mesh No. 100. For physical mixtures meloxicam and the carriers (PVP, HPMC, HPC and PEG) in 9:1 ratio were weighed, mixed well in a mortar and sifted through mesh No. 100.

Solvent deposited systems (SDS) of meloxicam were prepared employing lactose, soluble starch, microcrystalline cellulose (MCC), dicalcium phosphate (DCP) and silica gel as excipients in the drug and excipient ratios of 1:1 and 1:2. The solvent deposited systems were prepared by dissolving meloxicam in dichloromethane to obtain a clear solution. The excipient was then added to the solution and dispersed. The solvent was removed by evaporation at 40° under reduced pressure (8 in Hg Abs.) while mixing the contents. The mass obtained was powdered, mixed and sifted through a mesh No. 100. For physical mixtures meloxicam and excipients in 1:1 ratio were weighed, mixed well in a mortar and sifted through mesh No. 100.

Meloxicam tablets each containing 7.5 mg of meloxicam were prepared employing meloxicam (MX), MX-PVP (9:1), MX-HPMC (9:1) solid dispersions and MX-MCC (1:2) and MX-DCP (1:2) solvent deposited systems by conventional wet granulation method. Primogel (5%) acacia (2%) and lactose (q.s.) were used as disintegrant, binder and diluent respectively. The wet granules (mesh No. 12) were dried at 50° for 6 h. The dried granules were sized through mesh No. 16 and blended with disintegrant and lubricants. Tablet granulations were compressed into 100 mg tablets to a hardness of 5-7 kg/sq. cm on a Cadmach single punch tablet machine. In each case 100 tablets were prepared.

The tablets were tested for uniformity of weight as per IP (1996). Disintegration times were determined in a Thermonic tablet disintegration test machine (USP) using distilled water as the fluid. Hardness of the tablets was tested using a Monsanto hardness tester. Friability of the tablets was determined in a Roche friabilator.

An UV spectrophotometric method based on measurement of absorbance at 365 nm in phosphate buffer (pH 7.4) was used for the estimation of meloxicam.

The dissolution rate of meloxicam from the solid dispersions, solvent deposited systems and their tablet formulations in phosphate buffer of pH 7.4 (900 ml) was studied using a USP XXI 3-station dissolution rate test apparatus (Model DR-3, M/s Campbell Electronics) with a paddle stirrer at 50 rpm. Samples of dissolution medium (5 ml) withdrawn through a filter (0.45 μ) at different time intervals were assayed for meloxicam at 365 nm. The dissolution experiments were conducted in triplicate.

All the solid dispersions and solvent deposited systems were found to be fine and free flowing powders. Low coefficient of variation (<2%) in the percent

TABLE 1: DISSOLUTION RATE OF MELOXICAM FROM SOLID DISPERSIONS AND SOLVENT DEPOSITED SYSTEMS

Formulation	Percent meloxicam dissolved at 3 times (min) $\bar{x}$ ± s.d.			DE_{30}	K x 10^2
	10	30	60	(%)	($mg^{1/3}min^{-1}$)
Meloxican (MX)	11.0±1.1	28.7±1.2	39.4±0.5	15.6	0.8
MX-PVP (19:1) SD	17.7±1.5	69.1±2.3	92.6±1.6	32.8	4.8
MX-PVP (9:1) PM	10.8±1.0	29.6±0.3	38.2±0.7	16.2	1.0
MX-PVP (9:1) SD	85.5±1.2	98.5±1.3	99.2±1.1	77.4	15.2
MX-HPMC (19:1) SD	76.1±1.2	95.8±2.4	98.4±0.5	69.7	9.6
MX-HPMC (9:1) PM	11.3±0.9	29.0±1.0	39.7±1.3	15.9	1.2
MX-HPMC (9:1) SD	85.5±2.6	98.1±2.7	99.1±1.0	80.2	13.7
MX-HPC (19:1) SD	69.8±1.5	94.7±2.1	99.2±0.8	72.1	9.3
MX-HPC (9:1) PM	11.9±0.9	28.9±0.4	41.3±0.7	15.9	1.4
MX-HPC (9:1) SD	78.2±2.4	92.8±0.4	97.4±1.6	60.9	7.9
MX-PEG (19:1) SD	68.5±1.7	96.1±2.5	99.2±1.2	73.2	9.1
MX-PEG (9:1) PM	11.2±1.2	27.1±1.4	40.9±2.3	15.5	1.2
MX-PEG (9:1) SD	50.4±3.3	94.1±2.9	98.3±2.1	60.0	8.3
MX-lactose (1:1) PM	12.1±0.7	27.8±1.1	40.9±1.9	16.2	1.0
MX-lactose (1:1) SDS	34.1±1.3	64.3±2.3	90.9±1.8	39.8	3.9
MX-lactose (1:2) SDS	94.9±3.0	99.4±0.8	99.1±1.3	82.5	14.4
MX-soluble starch (1:1) PM	12.2±1.3	30.1±0.9	38.2±0.4	17.4	1.2
MX-soluble starch (1:1) SDS	18.4±0.5	51.9±2.5	78.4±1.4	26.7	1.4
MX-soluble starch (1:2) SDS	46.8±2.6	93.7±2.5	99.5±0.8	59.1	9.3
MX-MCC (1:1) PM	13.1±0.2	29.1±0.4	39.1±1.8	17.7	1.0
MX-MCC (1:1) SDS	57.5±1.5	91.1±4.3	98.6±1.5	60.9	9.1
MX-MCC (1:2) SDS	74.9±2.8	95.6±4.2	99.8±0.4	73.0	10.5
MX-DCP (1:1) PM	11.9±1.1	29.4±1.4	43.4±1.7	17.5	1.0
MX-DCP (1:1) SDS	39.5±2.1	86.4±1.9	96.6±1.7	50.9	7.0
MX-DCP (1:2) SDS	79.0±2.7	99.7±0.4	99.7±0.4	73.1	14.0
MX-silica gel (1:1) PM	11.9±0.7	27.1±0.4	40.1±0.4	16.4	1.0
MX-silica gel (1:1) SDS	16.3±0.5	72.0±1.3	92.4±2.7	34.5	4.5
MX-silica gel (1:2) SDS	64.1±2.1	96.2±1.3	99.4±0.8	69.5	9.9

Dissolution parameters of meloxicam from Solid Dispersion (SD), Solvent Deposited Systems (SDS) and Physical Mixtures (PM). K is Hixson-Crowell's cube root dissolution rate constant.

meloxicam content of the preparations indicated uniformity of drug content in each batch prepared.

The dissolution of meloxicam itself and from various dispersions (SD and SDS) obeyed Hixson-Crowell's cube root dissolution rate law. Plots of $[W_o^{1/3}-W^{1/3}]$ Vs time were found to be linear ($r>0.98$) where W_o is initial mass and W

is the mass remained at time 't'. The corresponding dissolution rates and dissolution efficiency [DE_{30}] values calculations as per Khan[4] are given in Table 1.

A marked increase in the dissolution rate and efficiency (DE) of meloxicam was observed with the solid dispersions and solvent deposited systems when compared to meloxicam itself and the corresponding physical mixtures. As concentration of the carrier in the solid dispersion was increased the dissolution rate was also increased with PVP and HPMC. Whereas with PEG and HPC the dissolution rate was decreased as the carrier concentration was increased. At 9:1 ratio of drug and carrier solid dispersions in PEG and HPC were found to be aggregated and granular. This aggregated granular form may be responsible for the observed decrease in the dissolution rate of these solid dispersions when compared to the corresponding solid dispersions prepared at 19:1 ratio of drug and carrier. Among the four carriers PVP gave highest improvement (19 fold) in the dissolution rate of meloxicam at 9:1 ratio of drug and carrier. The order of enhancement of the dissolution rate with various carriers was PVP>HPMC>PEG>HPC at 9:1 ratio of drug and carrier. The higher the dissolution rate and dissolution efficiency values observed with solid dispersions of meloxicam is due to the possible particle size reduction, improved wettability of hydrophobic drug particle by the presence of water soluble carriers, solubilising effect of the carrier and the possible conversion of crystalline drug into amorphous form. One or more of the above may be responsible for the higher dissolution rates observed with solid dispersions.

In the case of solvent deposited systems the order of increase in the dissolution rate of meloxicam with various excipients was MCC > DCP > silica gel > lactose > soluble starch at 1:1 ratio of drug and excipient. At 1:2 ratio of drug and excipient the order of increase in the dissolution rate was Lactose > DCP > MCC > Silica gel > Soluble starch. The higher dissolution rate observed with solvent deposited systems is due to micronization and deposition of the drug in miniscular form on the excipient as suggested by Monkhouse[3]. At lower proportion of excipient i.e. at 1:1, insoluble excipients (MCC, DCP, silica gel) gave higher dissolution rates and DE values than the soluble excipients (lactose and soluble starch). The soluble excipients might be dissolving rapidly leaving the particles of insoluble drug with poor dissolution. Whereas in the case of insoluble excipients as they remain suspended they give good contact between the deposited drug and the surrounding dissolution medium and hence higher dissolution rates.

At higher proportion of excipient i.e., at 1:2 ratio of drug and excipient the soluble excipient lactose also gave higher dissolution rate and DE value. This may be due to its hydrophilic nature which confers hydrophilic character to the solvent deposited systems. Whereas at 1:1 ratio of drug and excipient the lactose is not sufficient to impart hydrophilic character to the solvent deposited system. With all the excipients the dissolution rate was increased as the concentration of excipients was increased. Overall MCC and DCP gave highest improvement in the dissolution rate of meloxicam. 13.1 and 17.5 fold respectively at 1:2 ratio of drug and excipient.

All the tablets prepared were found to contain meloxicam within 100±5% of the labeled claim. Hardness of the tablets was in the range of 5-7 kg/sq.cm and was satisfactory. The percentage weight loss in the friability test was less than 1.2% in all the batches prepared. All the tablets, both formulated and commercial, disintegrated rapidly within 4 min fulfilling the official disintegration time specification for uncoated tablets. Tablets formulated employing solid dispersions and solvent deposited systems gave rapid and higher dissolution of meloxicam when compared to those formulated employing meloxicam itself and commercial brands (fig. 1). Tablets formulated employing solid dispersions gave higher

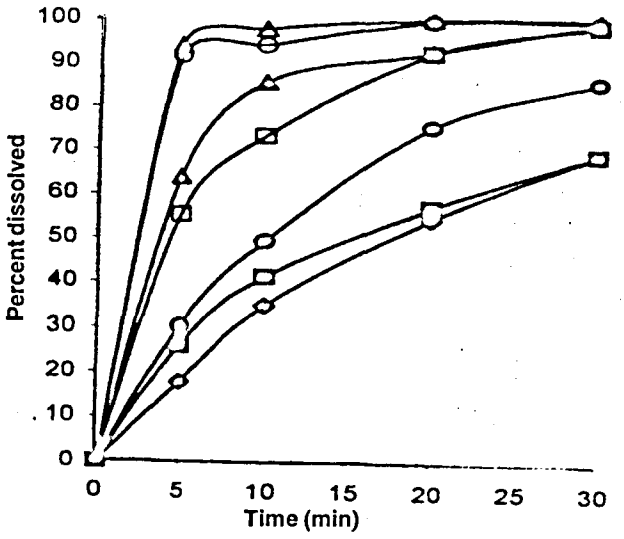

Fig. 1: Dissolution studies of meloxicam tablets
Dissolution profiles of meloxicam tablets formulated employing meloxicam (MX) alone (●), MX-PVP (○), MX-HPMC (△) solid dispersions (9:1) and MX-MCC (□) and MX-DCP (▲) solvent deposited systems (1:2). (■) and (◇) are two commercial brands of meloxicam tablets.

dissolution rates than those formulated employing solvent deposited systems.

Thus, the dissolution rate of meloxicam could be significantly enhanced by its solid dispersion in PVP, HPMC, HPC and PEG and also by solvent deposition on water soluble and insoluble excipients namely lactose, soluble starch, MCC, DCP and silica gel. When the solid dispersions in PVP and HPMC and the solvent deposited systems on MCC and DCP were formulated into tablets by conventional wet granulation method, the resulting tablets, apart from fulfilling all official and other specifications, exhibited higher dissolution rates of meloxicam.

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Synthesis and Antimicrobial Screening of a New Guggul Preparation

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The *in vitro* Antimicrobial activity of a new guggul preparation has been investigated against *Staphylococcus aureus, Staphylococcus epidermidis, Pseudomonas aeruginosa, Proteus vulgaris, Alcaligenes faecalis, Serratia marcesens, Escherichia coli, Micrococcus glutamicus, Bacillus thermodenitrificans, Bacillus subtilis, Bacillus pumilus.*The preparation containing a 5:10 proportion of guggul and coconut oil showed more antimicrobial activity than other preparations. Guggul and coconut oil when tested alone failed to show any antimicrobial activity.

Guggul is the oleo-gum resin obtained by the incision of the bark of the plant *Commiphora weighitici* Family Burseraceae. It contains 60% of resin, 30% of gum and 0.5% to 1.5% of volatile oil. Guggul is used as antiinflammatory, antirheumatic, hypolipidemic and hypocholesteremic drug[1]. The present investigation is aimed at preparing a new formulation containing guggul and coconut oil. The formulation prepared was screened for antimicrobial activity using agar-cup plate method[2].

The new formulation was prepared using different proportions of guggul and coconut oil that include 5:10, 6:10, 7:10 and 5:15 (w/v). Guggul and coconut oil mixtures were kept on a hot plate at 70° for 10 minutes with continuous stirring. One gram of the prepared preparation was dissolved in 5 ml of carbon tetrachloride (CCl_4) which was tested for antimicrobial activity against all organisms. Guggul and coconut oil were also dissolved separately in CCl_4, which was previously tested for antimicrobial activity against all organisms and found negative.

In vitro screening of antimicrobial activity was carried out against *S. aureus, S. epidermidis, P. aeruginosa, P. vulgaris, A. faecalis, S. marcesens, E. coli, M. glutamicus, B. thermodenitrificans, B. subtilis* and *B. pumilus.* The plates were inoculated with 18 h culture of respective microorganisms. The cups were made aseptically with a cork borer of 6 mm diameter and 50 µl of test solution was added into each cup using a micropipette under aseptic conditions.

The plates were kept in a refrigerator for 2 h to allow

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