In method A, the formation of the green coloured complex is due to the partial oxidation of 4-hydroxy group of meloxicam which ferric chloride. Ferrous ions thus produced form complexes with the reagents for divalent iron i.e., potassium ferricyanide. In method B, the reduction of FC reagent in the presence of 1 N NaOH gives a blue coloured chromogen, which may be molybdenum blue or tungsten blue. The results indicated that the proposed methods are simple, sensitive, reproducible and accurate and can be used for the routine determination of meloxicam in bulk and dosage forms.

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Comparative Evaluation of *In vitro* Performance of Commercial and Fabricated Sustained Release Diclofenac Sodium Tablets

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Ten commercial sustained release (SR) tablets of diclofenac sodium (DS) were evaluated for *in vitro* release characteristics in pH 7.4 medium. The rate and extent of drug release were highly variable for these tablets. Five batches of sustained and controlled release matrix tablet of DS were fabricated using polymers, like carboxymethyl cellulose (CMC) or carbopol 974P (Carbopol) alone or in combinations using different ratios, and were evaluated for physical characteristics and drug release performance. The results clearly indicated that batches prepared with admixed polymers exhibited more sustained and controlled release of DS in comparison to most of the commercial tablets. The treatment of data for zero-order, first-order and Higuchi's square root of time equations showed that all the fabricated tablets provided zero-order drug release profiles.

DS is a well-known NSAID, administered orally in the treatment of rheumatic diseases. Because of its short biological half-life and the hazards of adverse GI reactions, the development of oral sustained release formulations of this drug is highly desirable[1], so as to achieve improved therapeutic effect with negligible side effects and improved patient compliance. The use of controlled release technology in the formulation of pharmaceutical products has become increasingly important in the last few years[2] and many efforts have been made towards achieving sustained release formulations of DS[3-7]. Since many SR tablets of DS are available in the Indian market, we first evaluated the *in vitro* drug release characteristics of ten commercially available SR tablets of DS and found a large variation in their rate and extent of drug release. This prompted us to fabricate some optimized SR matrix tablets of DS using one or more polymers

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either alone or in combinations. Besides many other polymers, Carbopol[8] and CMC[9] are the two polymers extensively used in preparation of SR products of many drugs. So, an effort has been made in the present study to fabricate five different sustained and controlled release tablets of DS using polymers, like Carbopol and CMC (either alone or in combinations) and to compare them with ten commercial tablets for their *in vitro* drug release characteristics.

Commercial SR tablets of DS (Batches A, B, C, D, E, F, G, H, I and J, each containing 100 mg drug) manufactured by ten different companies in India were purchased from the market. DS was obtained as gift sample from Win-Medicare Ltd., Modipuram. Carbopol 974P and CMC were obtained from BF Goodrich Company, U.S.A. and GSC, Mumbai, respectively. All other chemicals used were of analytical grade.

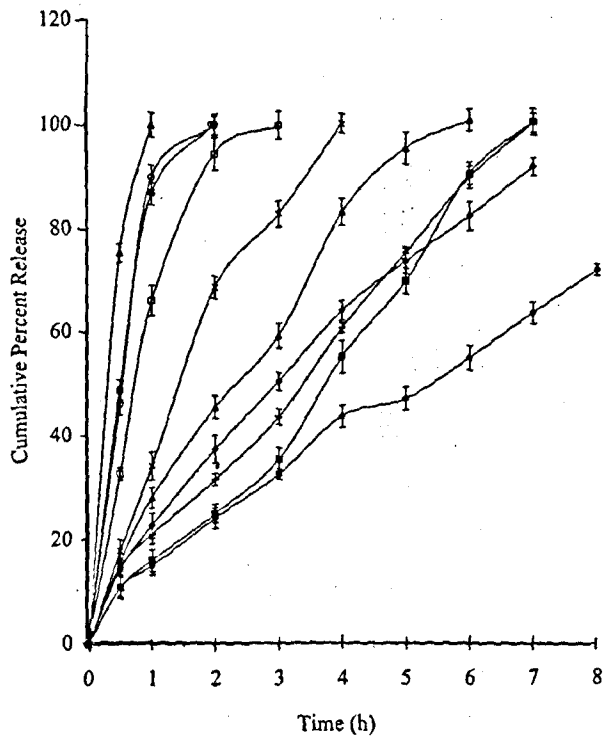

Fig. 1: *In vitro* release profiles of DS from commercial tablets

In vitro release profiles of DS from ten different commercial tablets in phosphate buffer (pH 7.4).These tablets are; A (-□-), B (-○-), C (-○-), D (-▲-) E (-◇-), F (-□-), G (-Δ-), H (-◊-), I (-✕-) and J (—). Each point represents the mean (n=5) of the experimental values and crossbars indicate ± S.D.

All the batches (K, L, M, N, and P) of matrix tablets were prepared by direct compression technique using 33.3% w/w of DS, 66.7% w/w of polymer and 1.0% w/w of magnesium stearate, in each tablet. The polymers used were; Carbopol (batch K), CMC (L) and combinations of CMC and Carbopol in ratios 50:50 (M), 25:75 (N) and 75:25 (P). Each batch is of 200 tablets. All the ingredients were passed through sieve No. 85, blended uniformly and compressed on a Manesty E2 tabletting machine using 10 mm standard flat surface punches at a pressure that gave Monsanto hardness of 8 kg/cm^2. All the fabricated tablets were evaluated for thickness, weight variation, hardness, drug content uniformity and *in vitro* drug release characteristics as per USP XXI monograph.

All the commercial and fabricated tablets were evaluated *in vitro* (5 runs for each batch) on an USP XXI

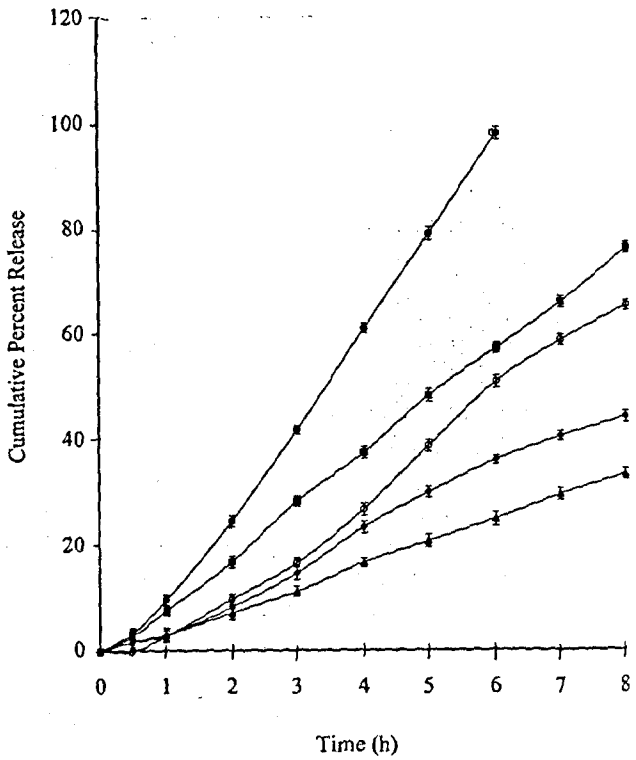

Fig. 2: *In vitro* release profiles of DS from five fabricated tablets

In vitro release profiles of DS from five different fabricated tablets in phosphate buffer (pH 7.4).These are tablets are represented by k (-□-), L (-○-), M (-○-), N (-▲-) and P (-◇-). Each point represents the mean (n=5) of the experimental values and crossbars indicate ± S.D.

TABLE 1: KINETICS AND EXTENT OF *IN VITRO* DS RELEASE

S. No.	BATCHES	r values			Cumulative percent release (%) ± S.D. (n = 5)	
		Zero Order	First Order	Higuchi	0 –5 h	5-8 h
1	A	0.9953	0.9839	0.9385	69.64* ± 2.49	100.00 ± 2.54
2	B	0.9229	0.8918	0.9871	100.00*±1.98	-
3	C	0.9080	0.8861	0.9806	100.00*±1.87	-
4	D	0.9652	0.8184	0.9375	100.00*±2.12	-
5	E	0.9873	0.7886	0.9885	73.50±2.39	91.26*±1.73
6	F	0.9222	0.8176	0.9907	100.00*±2.67	-
7	G	0.9855	0.7980	0.9821	95.00*±3.13	100.00±2.07
8	H	0.9924	0.8430	0.9819	47.03*±2.21	71.58*±1.11
9	I	0.9927	0.8379	0.9835	100.00*±1.87	-
10	J	0.9976	0.8220	0.9651	75.09±1.17	100.00±1.81
11	K	0.9994	0.8822	0.9521	48.37*±1.21	76.12*±1.01
12	L	0.9968	0.9010	0.9292	78.94*±1.23	100.00±1.17
13	M	0.9915	0.9382	0.9174	38.85*±1.10	65.14*±0.96
14	N	0.9990	0.9297	0.9474	20.85*±1.18	33.25*±1.09
15	P	0.9946	0.9259	0.9426	30.00*±1.01	44.18*±1.11

- Denotes not applicable. Test for significance (t – test) was performed for all the products in reference to a standard marketed product J (Voveran®–SR). * Denotes statistical significance at $P< 0.05$.

dissolution apparatus II for 8 h using 900 ml of pH 7.4 phosphate buffer maintained at 37 ± 0.1° and stirred at 100 rpm. Five millilitres of samples withdrawn at different time intervals were analysed on a Jasco UV/VIS Spectrophotometer (model 7800) at 275 nm after suitable dilution. Samples drawn were replaced by equal volumes of prewarmed (37±0.1°) fresh buffer. The actual drug content in the samples was read from a calibration curve.

The variation in the thickness, weight, hardness and drug content uniformity values for all the five batches of fabricated tablets, in reference to average values for each parameter, were found within the official limits.

The *in vitro* drug release profiles for commercial and fabricated tablets are shown in figs. 1 and 2, respectively and % drug released between 0-5 h and 5-8 h in Table 1. Out of 10 commercial SR tablets tested, tablets B, C, D and F performed like fast release dosage forms, as they delivered 90% or more drug within one or two h. Tablets A, E and J were almost similar in their *in vitro* performance and exhibited slow drug release as compared to B, C, D and F. Drug release from tablets J and E were more linear. The most sustaining effect on drug release was observed for tablet H, whereas *in vitro* drug release from tablet G was of intermediate nature out of all the commercial formulations evaluated. The above results clearly indicate a large variation in drug release characteristics of all the ten commercial tablets, which may result into great variation in their therapeutic performance.

The *in vitro* results (Table 1, fig. 2) observed for the fabricated tablets show that except for tablet L, which gave little higher rate and extent of drug release, the other four tablets (K, M, N and P) provided well controlled and sustained drug release profiles. The most sustaining effect was observed for tablets N and P.

In order to investigate the release mechanism, the data were fitted to models[10] representing zero-order, first-order and Higuchi's square root of time and equation[10]

$M_t/M_\infty = Kt^n$, where M_t/M_∞ represent fraction of drug released after time t, K a coefficient and n release exponent. The linear regression analysis shown as r values in Table 1 demonstrate that all the five fabricated tablets followed zero-order drug release kinetics. Though commercial tablets A, G, H, I and J also exhibited zero-order drug release kinetics, release rates from them were much faster as compared to fabricated tablets. The n values for fabricated tablets were in the range of 0.65 – 0.90 indicating non-Fickian drug release. For commercial tablets n values were 1.15 for J and > 1.15 for others.

The present investigation thus established the usefulness of evaluating the existing commercial SR formulations of DS for their *in vitro* performance and was concluded that the potential sustained and controlled release matrix tablets of DS could be prepared by incorporating polymers like CMC, Carbopol and their combinations in optimised ratio.

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Estimation of Nicotine from Gutkha, a Chewable Tobacco Preparation by a New HPTLC Method

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Nicotine is one of the highly toxic and addictive chemicals, belonging to tobacco alkaloids. In the present work, a HPTLC method was developed for the estimation of nicotine in different brands of *Gutkha* available in local market. Diethyl ether extracts of standard nicotine and the sample solutions were spotted on pre-coated TLC Silica gel G60 F_{254} plated and developed using chloroform:methanol:ammonia (60:5:1 v/v) as mobile phase. Densitometric scanning was performed at 255 nm. The linearity was found to be in the concentration range of 200-1000 ng/spot with correlation coefficient of 0.996. The method was validated for precision, repeatability and accuracy. Twenty different brands of *Gutkha* were analysed for the nicotine content and the results were compared with the nicotine content estimated by an UV-Spectrophotometric method. The content of nicotine in different brands of *Gutkha* was found to be in the range of 0.1 to 0.5% w/w.

Gutkha is a chewable tobacco preparation, containing arecanut, lime, catechu, flavors, permitted spices, saffron and tobacco. Tobacco was formerly used in medicine as sedative, antispasmodic, antiinflammatory, laxative, emetic and abortificient[1]. It's use has been super-

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