ISSN 1110-5089

Zagazig J. Pharm. Sci., December 2004
Vol. 13, No. 2, pp. 22-28

PREPARATION AND EVALUATION OF TOPICAL FORMULATIONS OF MELOXICAM

Ahmed M. Othman and Ahmed M. Sabati
Department of Pharmaceutics, Faculty of Pharmacy, Sana'a University, Sana'a, Yemen

ABSTRACT

The present work was carried out to prepare topical formulae of meloxicam (0.5%w/w of base) using different ointment and gel bases. The drug release from these bases was evaluated in phosphate buffer pH 7.4. Release data showed complete drug release from the water soluble base after 120 minutes where other ointment bases exhibited inappropriate drug release within 150 minutes. The effect of different enhancers such as sodium lauryl sulfate (SLS) and dimethyl formamide (DMF) on the release pattern of the drug from both hydrocarbon and hydrophilic ointment bases revealed a slight increase of drug release with increasing concentration of enhancers. On the other hand, the drug release from various gel bases was in the following order: Methylcellulose (MC) > Carbopol-934 >hydroxypropylmethylcellulose (HPMC) > Tragacanth >sodium alginate. Furthermore, incorporation of enhancers such as Tween 80 in concentration of 5% to both MC and HPMC bases improved drug release as well as 50.37 and 32.85 percent were released after 150 minutes respectively. Addition of few drops of triethanolamine to the previous bases containing 5% Tween 80 exhibited the most efficient gel bases in which the optimal drug release was attained after 120 minutes. Finally, ethanol gel containing MC and HPMC as gelling agents showed complete drug release within 120minutes. Thus, topical application of meloxicam in the MC and HPMC gel bases may be of potential use for local analgesic and anti-inflammatory activity.

INTRODUCTION

Nonsteroidal anti-inflammatory drugs (NSAIDs) are a class of compounds characterized by a similar pharmacological profile encompassing anti-inflammatory, analgesic and antipyretic activities. They are indicated for the treatment of musculo-skeletal disorders and other syndromes involving pain[1,2] Despite their well-known therapeutic efficacy, NSAIDs have the potential to cause adverse reactions, especially with regard to the digestive system and the kidney[3,4]. The most common adverse events related to the use of NSAIDs involve the gastrointestinal (GI) tract, and include a range of disorders, from functional problems - such as dyspepsia, heartburn and abdominal discomfort - to GI hemorrhage, peptic ulcer and perforation. Epidemiological studies have shown that approximately 10-20% of NSAID-treated patients have gastro duodenal erosions or ulcers detected at endoscope, and 60% of those with serious GI complications are on long-term NSAID therapy[5,6,7]

The topical administration of an anti-inflammatory agent at inflamed site will alter the potential advantage of delivering drug directly to the surface area and producing a locally high concentration of the drug.

The present work is an attempt to prepare meloxicam topically to be used as anti-inflammatory analgesic with the possibility of less systemic side effects. Also, in-vitro evaluation of drug release from various ointment and gel bases and the effect of enhancers on the drug release were studied.

MATERIALS AND METHODS

Materials:

1. Meloxicam: was supplied from Sheba Pharmaceutical Co., Yemen
2. White wax, white petrolatum, wool alcohol, cetostearyl alcohol, stearic acid, were obtained from Yemen Drug Co., (YEDCO) Yemen.
3. Carbopol-934, methylcellulose, hydroxypropyl-methylcellulose, eudragit-L-: were obtained from Chemical Industrial Development (CID), Co., Egypt.
4. Sodium alginate, cetyl alcohol, propylene glycol 400 and 4000, sodium lauryl sulphate, and Tween80: were gifts from SHAPHACO, Yemen.
5. Sodium hydroxide, potassium hydrogen orthophosphate: were purchased from BDH Chemicals, England
6. Other chemicals and reagents were of analytical grades.

Equipments:

1. Ultraviolet Spectrophotometer: Shimadzu UV-1601PC, Japan
2. USP-dissolution tester: Pharma test, type PTW, Germany.
3. Constant magnetic stirrer: Cat (M15), China
4. Electronic balance: Sartorius, Germany

Preparation of Different Ointment Bases Containing Meloxicam:

A- Preparation of ointment bases:

Four types of ointment bases were prepared: hydrocarbon, absorption, emulsions and water-soluble bases[8,9].

1-Hydrocarbon ointment base:

R/

White wax	95g
White petrolatum	5 g

2-Absorption base:

(U.S.National Formulary):

R/

Wool alcohol	6 g.
Hard paraffin	24 g.
White soft paraffin	10 g.
Liquid paraffin	60 g.

The ingredients were mixed, heated gently on a water bath with stirring until homogenous and then triturated until cold.

3- Emulsion bases:

a- Hydrophilic ointment base (O/W):

R/	
Cetyl alcohol	15 gm.
Beeswax	1 gm.
Sodium lauryl sulphate	2 gm.
Propylene glycol	10 gm.
Water ad	72 gm.

b- Vanishing Cream (O/W):

R/	
Stearic acid	13 g
Stearyl alcohol	1 g
Cetyl alcohol	1 g
Glycerin	10 g
Methylparaben	0.1 g
Propylparaben	0.05 g
Potassium hydroxide	0.9 g
Purified water qs ad	100 g

The oily phase and aqueous phases were heated to about 65°C. The oil phase was added slowly to the aqueous phase with trituration to form emulsion, then cooled at room temperature with trituration until congealed.

4-Water soluble base:

R/	
Polyethylene glycol 400	60%
Polyethylene glycol 4000	40%

This base was prepared by mixing and heating on a water bath at 60°C. Meloxicam was levigated with few mls of the melted base .Then the remaining melted base was gradually added to the levigated mixture with stirring until congealing

All the pervious bases were prepared. Then, Meloxicam was incorporated into each base so as to 0.5% w/w.

B- Preparation of the gel bases:

The calculated amounts of polymers were sprinkled gradually into the 25 ml distilled water containing 125 mg of meloxicam, with or without enhancers or solubilizers, placed in a 100 ml beaker and stirred with a glass or magnetic stirrer at a high speed. Stirring was continued until no lumps were observed, and left aside for 24 hours at room temperature.

1- The gelling agents used involved:

Carbopol-934, hydroxypropylmethylcellulose (HPMC), methylcellulose (MC), tragacanth and sodium alginate in concentration of 4% w/w of solvent [10,11].

2- Preparation of meloxicam gels containing: MC and HPMC as gelling agents in concentrations of 3 and 4% w/w of solvent used with different concentrations of Tween-80 as enhancer was done.

3- Meloxicam gels containing MC and HPMC as gelling agents in concentrations of 3, and 4% w/w of solvent with 5% Tween 80 and a few drops of Triethanolamine as solublizer and enhancer were also prepared.

4- Ethanol gel:

1- Meloxicam 0.5% w/w was dissolved in 25 ml of a mixture of : ethanol: water : glycerin (40; 40:20).

2- The calculated amount of Methyl cellulose and Hydroxypropyl methyl cellulose was sprinkled gradually into 25 ml of ethanol drug solution containing 5% Tween 80 and few drops of triethanolamine, and stirred with a magnetic stirrer till a homogenous mixture was obtained and then left aside for 24 hours to break the foams[12].

III- Determination of Drug content:

Accurately weighed samples of creams and gels were placed in volumetric flask, diluted to a certain volume with water containing few drops of triethanolamine and stirred for 30 minutes .The samples were then filtered and measured spectrophotometrically at 354 nm for determination of drug content[13]. All the experiments were performed in duplicates. The results were acceptable between 96-104% of theoretical values.

IV-Determination of Drug Release from Different Bases:

This study was carried out using USP dissolution tester.

The drug-loaded base consisting of 2 g base containing 10 mg meloxicam was placed in the basket covered with fabricated cotton.

The baskets were dipped in 300 ml phosphate buffer pH 7.4 .The release study was carried out at 37°C and stirring speed of dissolution tester was 50 rpm. 5-ml sample was withdrawn each time, from the vessels and filtered. Sampling was carried out after 15, 30, 45, 60, 90,120, and 150 minutes from the beginning of the test, and 5ml of phosphate buffer were added to vessels to replace the withdrawn sample. Each sample was suitably diluted, if necessary using the same buffer and analyzed spectrophotometrically at 354 nm for Meloxicam against a blank. The blank was prepared according to the same procedure but using a plain base. All the release experiments were run in duplicates.

RESULTS AND DISCUSSION

The dissolution profile of meloxicam from different ointment bases was studied. It was watched from table 1 and fig.1 that, the drug release from hydrocarbon, absorption and hydrophilic ointment bases was nil after 150 minutes, while 27.34 percent of drug released from vanishing cream base (o/w cream) within the same time. The hindered drug release may be attributed to high affinity of water insoluble drug to white petrolatum present in the previous formulations. On the other hand, water soluble ointment base showed complete drug release within 120min. Generally, the higher percentage of polyethylene glycol 400 as a water-soluble component was attributed to the highest drug release. Therefore, the drug release is highly affected by the nature and the composition of the base [14].

Zagazig J. Pharm. Sci., December 2004
Vol. 13, No. 2, pp. 22-28

The effect of enhancers on drug release from these bases was investigated, it was observed from table 2 and fig.2 that, the hydrocarbon ointment base with 0.5 and 1% sodium lauryl sulfate (SLS) and dimethyl formamide (DMF) showed no drug release, where 3 & 5% w/w exhibited slightly drug release. Upon increasing the concentrations of both enhancers up to 10% w/w, the drug release was slightly increased as 9.88 and 10.68 percent from hydrocarbon base within the same period of time.

Eventually, the tried concentrations of DMF as well as 0.5, 1%w/w of hydrophilic ointment base exhibited nil drug release after 150 minutes. On using 3,5 and 10% of DMF, the percentage of drug release was 3.76 ,11.7 and 15% within the same time respectively. In conclusion, DMF exhibited higher percentage of drug release both hydrocarbon and hydrophilic ointment bases. This might be attributed to possible change in the drug solubility in bases produced by the additive [15].

The release pattern of meloxicam from different gel bases (in concentration of 4%) viz.,: Methylcellulose, Carbopol- 943, Hydroxypropyl methylcellulose, Tragacanth, and sodium alginate were tried. It was found from table 3 and fig. 3 that ,the highest drug release was watched from methylcellulose and the least drug release was from sodium alginate gel bases. The release of meloxicam from traditional gel bases was in the following descending order: MC > Carbopol-943 > HPMC > Tragacanth > sodium alginate. 16.84, 15.30, 13, 10.55, and 9.09 percent of drug were released after 150 minutes respectively.

All gel bases exhibited less extent of drug release, this might be attributed to the high viscosity of gel bases and also the drug entrapment efficiency of the net work structure of these gel bases and consequently retarding the drug release[16]

On trying different concentrations of MC and HPMC gels table 4 and fig.4 showed that, the higher the concentration of the gel base the lower the extent of drug release. Thus, 34.55, 27, and 16.84 percent of drug were released from 2, 3, and 4 % of MC gel where 31.71, 24.77, and. 13 percent were released from HPMC of the same aforementioned concentrations respectively.

The effect of different concentrations of an enhancer such as Tween 80 (1, 3, and 5% w/w of gel base) on drug release from methyl cellulose and hydroxypropyl methylcellulose gel bases was evaluated. Table 5 and fig.5 revealed that, the higher the concentration of enhancer, the higher the extent of drug release. Methylcellulose gel with different concentrations of Tween 80 expressed higher drug release than that obtained from Hydroxypropyl methylcellulose gel with the same concentrations of Tween 80. Thus, 50.37 and 32.85 % of drug were released from MC and HPMC with 5% Tween 80 after 150 minutes respectively. Therefore, The effect of Tween 80 as an enhancer on the release of meloxicam from both gel bases might be explained: first, by decreasing viscosity of the gel which enables drug release, and the second, Tween 80 is a surface active agent which may increase the solubility of drug in the buffer medium. This in agreement with that obtained by other authors [8, 9, 17].

Addition of few drops of triethanolamine (TEA) to the aforementioned bases showed complete drug release from 3%MC and 96% from 3% HPMC containing 5% Tween 80 after 150 minutes where 93 and 85.94 percent were released from 4% MC and 4% HPMC respectively. This might be attributed to the enhancing and solublizing effect of triethanolamine[18].

Finally, ethanol gel containing MC and HPMC in concentration of 3 and 4% with a few drops of TEA exhibited the optimal drug release where 100percent of drug was released after 90min and 120min respectively. Hence, 3% MC or HPMC ethanol gel is the most efficient gel bases to be used locally for their analgesic and anti-inflammatory effects.

CONCLUSION

Topical application would allow the administration of meloxicam for those patients who can not tolerate the oral drug because of its gastrointestinal adverse effects. Thus, topical application of meloxicam gel containing 3 % of either MC or HPMC with 5% Tween 80 and few drops of triethanolamine may be of potential use for local analgesic and anti-inflammatory effects. On the other hand, ethanol gel containing 3% or 4% of MC and HPMC as gelling agents also may be considered of a potential use.

Table 1: Percentage Meloxicam Released from Different Ointment Bases

Ointment bases	Time Intervals(Minutes)					
	15	30	60	90	120	150
Hydrocarbon	No drug release					
Absorption*	No drug release					
Hydrophilic	No drug release					
PEG*** (±SD**)	46.67 ±0.32	49.49 ±0.69	65.58 ± 0.58	88.98 ± 0. 22	100 ±0.7	--
Vanishing cream(±SD)	5.40 ± 0.7	10.55 ± 0.63	14.55 ± 0.6	18.90 ± 0.42	24.49 ± 0.65	27.34 ± 0.62

Absorption*= NF
PEG***= Polyethylene glycol ointment base
SD**= Standard deviation

Table 2: Percentage meloxicam released from hydrocarbon and hydrophilic ointment bases containing different concentrations of enhancers:

Ointment bases	(%w/w) Enhancer	Time intervals (min) 15	30	60	90	120	150
Hydrocarbon (±SD)	3%SLS	--	--	--	0.789 ±0.069	1.82± 0.08	2.14 ± 0.14
	5%SLS	0.66 ±0.06	1.96 ± 0.14	2.46 ± 0.54	2.77 ±0.43	3.02 ±0.53	4.39 ±0.27
	10%SLS	2.21 ±0.01	3.58 ± 0.07	4.77 ±0.07	6.66 ±0.04	8.68 ± 0.08	9.88 ± 0.02
	3%DMF	--	--	1.21 ± 0.19	1.822 ± 0.17	2.43 ±0.27	2.85 ± 0.15
	5%DMF	1.34 ±0.11	2.24 ±0.24	3.56 ±0.36	4.31 ± 0.11	4.87 ± 0.27	6.55 ± 0.25
	10%DMF	2.11 ±0.11	3.42 ± 0.42	5.21 ± 0.21	7.30 ± 0.30	8.25 ±0.25	10.68 ± 0.68
Hydrophilic (±SD)	3%DMF	0.73 ± 07	1.52 ± 0.05	2.186 ±0.034	2.31 ±0.09	2.976 ±0.07	3.765 ± 0.04
	5%DMF	2.09 ±0.1	2.95 ± 0.25	5.09 ± 0.2	8.50 ± 0.4	9.60 ± 0.15	11.70 ± 0.10
	10%DMF	2.63 ±0.17	3.87 ±0.13	6.55 ±0.55	10.00 ±0.2	13.52 ±0.48	15.06 ± 0.54

SLS=Sodium lauryl sulfate
DMF=Dimethylformamide
SD= standard deviation

Table 3: Percentage meloxicam released from different gel bases in a concentration of 4% w/w.

Gel bases	Time intervals (min) 15	30	60	90	120	150
Sod alginate (±SD)	1.86 ±0.4	2.6 ± 0.3	3.98 ±0.02	5.65 ±0.05	7.18 ±0.04	9.09 ± 0.02
Methylcellulose (±SD)	1.8 ±0.05	4.91 ±0.03	8.51 ±0.06	11.48 ±0.07	14.77 ±0.07	16.84 ±0.06
HPMC(±SD)	2.98 ±0.48	4.85 ±0.1	6.01 ±0.31	8.80 ±0.3	10.90 ±0.10	13.00 ±0.5
Tragacanth(±SD)	2.09 ±0.19	3.80 ±0.3	5.05 ±0.4	7.53 ±0.18	9.11 ±0.31	10.55 ±0.25
Carbopol934 (±SD)	3.06 ±0.18	5.16 ±0.34	7.05 ±0.29	10.43 ±0.33	12.76 ±0.27	15.30 ±0.31

Table 4: Percentage meloxicam released from different concentrations of methylcellulose and hydroxypropylmethylcellulose gel.

Gel bases	Conc.	Time intervals (min): 15	30	60	90	120	150
Methylcellulose (±SD)	2%	3.78 ±0.3	9.88 ±0.12	15.66 ±0.34	22.58 ±0.17	28.92 ±0.22	34.55 ±0.20
	3%	3.5 ±0.5	8.90 ±0.3	13.26 ±0.26	19.78 ±0.22	23.77 ±0.33	27.05 ±0.55
	4%	1.8 ±0.05	4.91 ±0.03	8.51 ±0.06	11.48 ±0.07	14.77 ±0.07	16.84 ±0.06
HPMC(±SD)	2%	4.25 ±0.15	8.75 ±0.63	13.64 ±0.59	19.45 ±0.55	25.76 ±0.60	31.71 ±0.77
	3%	2.90 ±0.2	6.67 ±0.63	10.11± 0.59	14.95 ±0.55	19.02 ±0.78	24.77 ±0.77
	4%	2.98 ±0.48	4.85 ±0.10	6.01 ±0.31	8.80 ±0.3	10.90 ±0.1	13.00 ±0.5

Table 5: Percentage meloxicam released from methylcellulose and hydroxypropylmethylcellulose gel bases containing different concentrations of Tween 80.

Gel bases	% Tween 80	Time intervals (min): 15	30	60	90	120	150
Methylcellulose (±SD)	1%	15.98 ± 0.38	24.66 ±0.78	29.92 ± 0.85	31.70 ±0.76	33.32 ±0.68	37.59 ±0.51
	3%	19.17 ± 0.30	28.56 ±0.77	34.810 ±0.77	40.32 ±0.52	45.01 ±0.59	48.13 ±0.25
	5%	30.82 ± 0.18	41.01 ±0.11	44.32 ±0.13	46.91 ±0.11	4887 ±0.13	50.37 ±0.17
Hydroxypropyl methyl cellulose (±SD)	1%	12.66 ± 0.14	19.66 ±0.34	21.69 ±0.19	24.10 ±0.3	23.89 ±0.24	26.59 ±0.29
	3%	14.75 ± 0.25	19.72 ±0.30	24.43 ±0.37	24.02 ±0.22	25.29 ±0.19	28.65 ±0.35
	5%	19.49 ± 0.51	22.54 ±0.46	24.29 ±0.56	27.82 ±0.68	30.18 ±0.38	32.85 ±0.35

Table 6: Percentage meloxicam released from methylcellulose and hydroxypropyl methyl cellulose gel bases containing 5% Tween 80 and few drops of triethanolamine.

Gel bases	Conc. of base.	Time intervals (min): 15	30	60	90	120	150
Methyl-cellulose (±SD)	3%	27.54 ±1.04	44.43 ±1.43	63.66 ±1.14	76.90 ±1.10	94 ± 1.00	100 ± 2.00
	4%	16 ± 1.0	30 ± 1.5	52 ±1.6	68 ±1.2	81 ±1.5	93 ±1.8
HPMC (±SD)	3%	17.56 ±0.56	38.33 ±0.33	58.66 ±0.34	71.01 ±0.60	84.81 ±0.79	100 ± 0.60
	4%	21.89 ±0.56	35.55 ±0.75	47.88 ±0.82	62.58 ±0.72	70.55 ±0.75	87.94 ± 0.65

Table 7: Percentage meloxicam released from ethanol gel containing 3 and 4% methylcellulose and hydroxypropyl methyl cellulose.

Gel bases	Conc. of base	Time intervals (min): 15	30	60	90	120	150
Methylcellulose (±SD)	3%	26.65 ±0.65	52.43 ±0.43	70.90± 0.9	100 ± 1.0	--	--
	4%	24.25 ±0.45	40.75 ±0.25	58.80± 0.20	70.81± 0.39	100± 0.60	--
HPMC(±SD)	3%	33 ±1.0	53.25 ±1.25	78.8 ±1.8	100 ± 2.2	--	--
HPMC(±SD)	4%	22.65 ±0.65	42.63 ±0.87	51.84± 0.46	67.93± 0.53	100 ± 0.50	--

Zagazig J. Pharm. Sci., December 2004
Vol. 13, No. 2, pp. 22-28

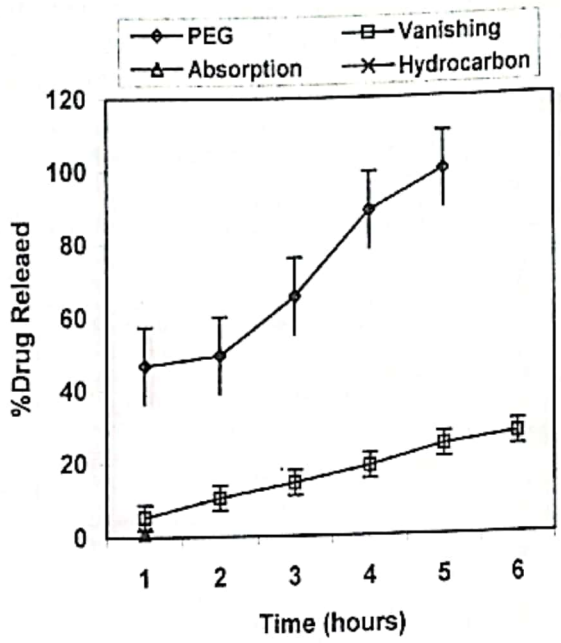

Fig. 1: *In-vitro* release of meloxicam from different ointment bases into phosphate buffer pH 7.4.

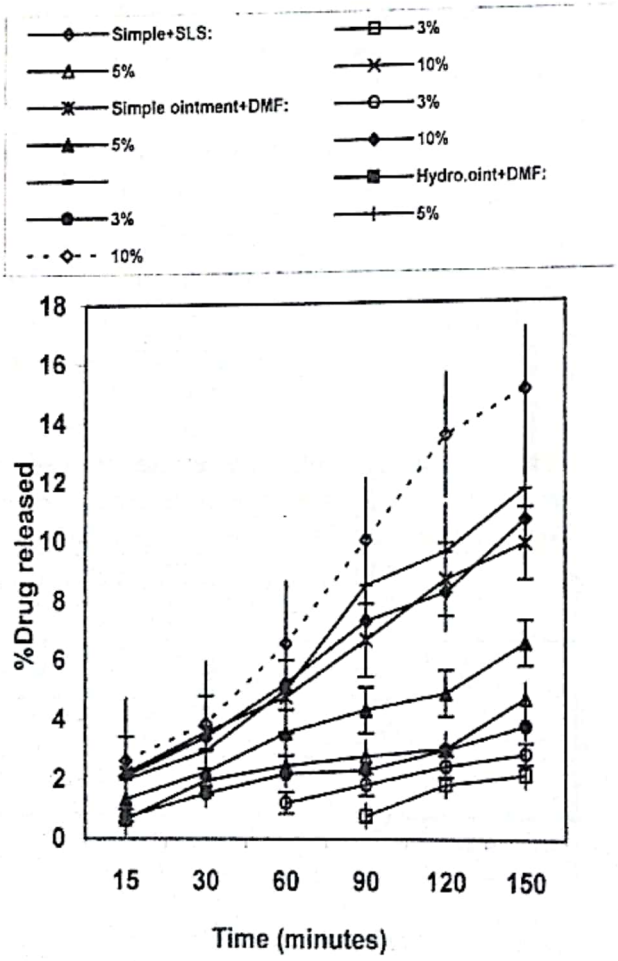

Fig. 2: *In-vitro* release of meloxicam from hydrocarbon and hydrophilic ointment bases containing different concentration of enhancers into phosphate buffer pH 7.4.

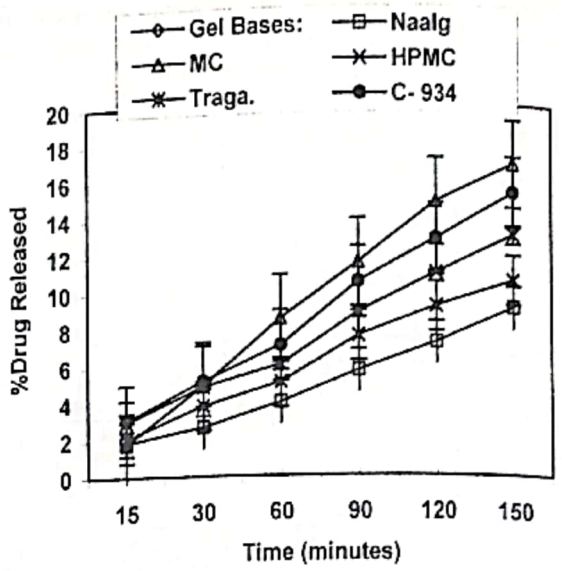

Fig. 3: *In-vitro* release of meloxicam from different gel bases into phosphate buffer pH 7.4

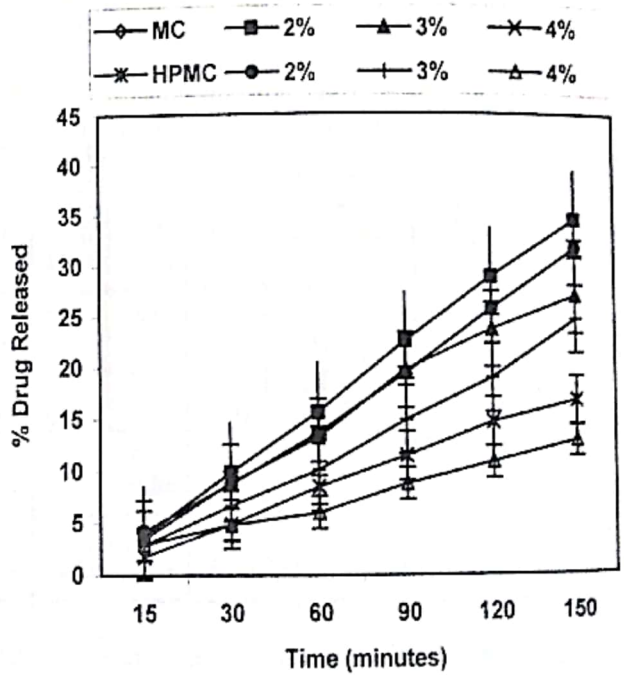

Fig. 4: *In-vitro* release of meloxicam from different concentration of methylcellulose and hydroxypropyl-methylcellulose into phosphate buffer pH 7.4

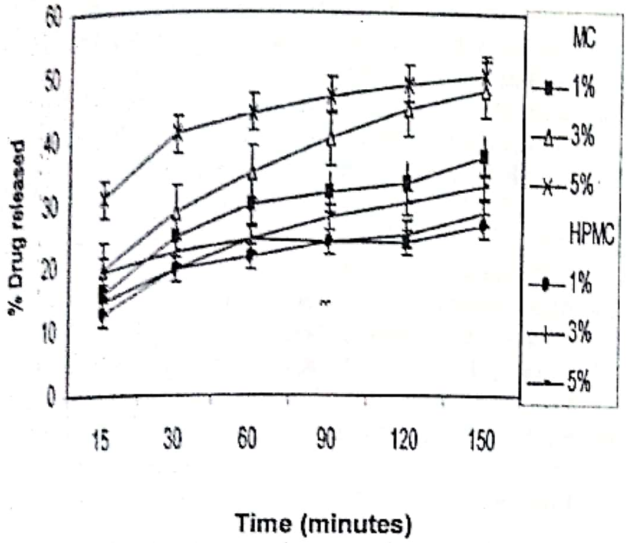

Fig. 5: *In-vitro* release of meloxicam from methylcellulose and hydroxypropylmethylcellulose gel containing different concentrations of Tween 80 into phosphate buffer pH 7.4

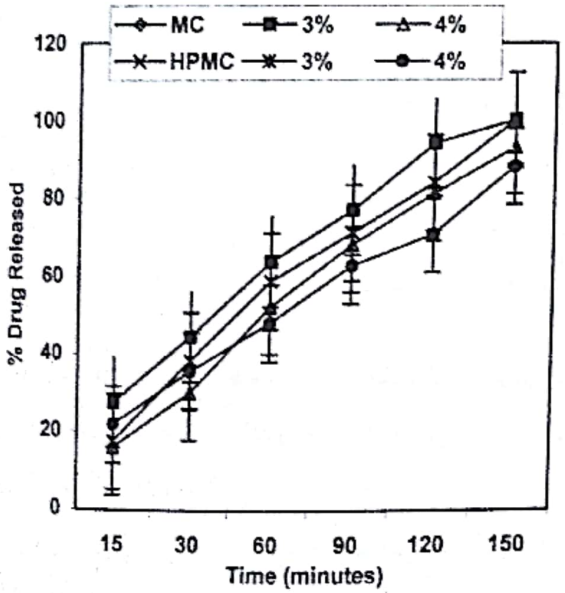

Fig. 6: *In-vitro* release of meloxicam from methylcellulose and hydroxypropylmethylcellulose gel bases with 5% tween 80 and few drops of triethanolamine into phosphate buffer pH 7.4

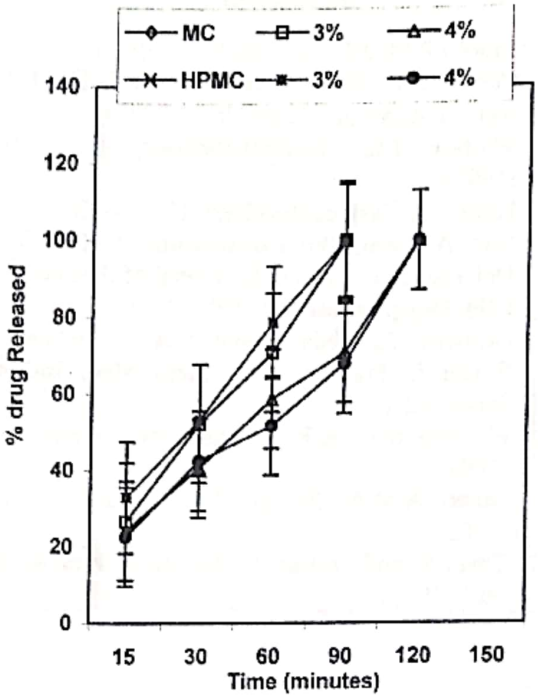

Fig. 7: *In-vitro* release of meloxicam from ethanol gel containing 3 and 4% of methylcellulose and hydroxypropylmethyl cellulose and few drops of triethanolamine into phosphate buffer pH 7.4.

Zagazig J. Pharm. Sci., December 2004
Vol. 13, No. 2, pp. 22-28

REFERENCES

1. Brooks P.M, **J.Med** : 324, 1716 (1991) .
2. Carroll G.L.; Howe L.B.; Peterson K.D., **J Am. Vet. Med. Assoc.**: 226(6):913 (2005)
3. Wallace J.L., **Gastroenterology**: 112, 1000 (1997).
4. Laine .L., **Gastroenterology** :120,564 (2001).
5. Gary A.Green, **Clin. Cornerstone**: 3, 50 (2001)
6. Del Tacca M., Colucci R., Fornai M.,Blandizzi C., **Clin. Dryg. Invest.**, 22, 799 (2003)
7. Girawan D., Abdurachman S.A., Djumhana A., Roslia J., Pramudiyo R., **Acta Med. Indones**: 36(4):202 (2004)
8. El –Shaboury K.F. Master thesis, Cario Univ. (1992).
9. Sabati A.M.A. Ph. D. Thesis, Zagazig Univ., (2002).
10. Tayel S. and Osman A., **Egypt. J. Pharm. Sci.**, 36,1 (1995)
11. Takeeda T., Halakeyam Y., Kitaura I., Luamoto Y., Morimoto K., Yasuda M., Nakamoto Y., Morisaka K., Danjo K., amd Otsuka A., **Int. J. Pharm.**,41, 21 (1988)
12. GiannaKou S.A., Dallas P.P., Rekkas D.M., Choules N.H., **Int. J. Pharm.**, 125, 7 (1995).
13. British Pharmacopiea, vol. 1, p. 936 (1999).
14. Idson B., **Drug Metab. Rev.**, 14, 207 (1983)
15. White Worth C.W., and stephenson R.E., Canad. **J. Pharm. Sci.**, 10, 89 (1975).
16. Abd.El-Bary A.,Tayel S., Amine S., and Osman A., **Egypt. J. Pharm. Sci.**, 33, 1031 (1992).
17. Desai S.J., Simonella A.P., and Higuchi W.I., **J. Pharm. Sci.**,54,1459 (1965).
18. Kibbe A.H., Hand book of Pharmaceutical Excipients, third Ed., Pharmaceutical Press, London, U.K. (2000).

Accepted: Sept. 06, 2004
Received: Nov. 20, 2004

صياغة وتقييم عقار الميلوكسيكام موضعياً

احمد محمد عثمان – احمد محمد سباتي

قسم الصيدلانيات – كلية الصيدلة – جامعة صنعاء – صنعاء – اليمن

تتضمن هذة الدراسة تحضير عقار الميلوكسيكام موضعياً باستخدام قواعد مختلفة من المراهم والهلاميات.

حيث وجد أن انطلاق العقار كان كاملاً من القاعدة المرهمية عديدة الأيثلين , أما انطلاق العقار من القواعد المرهمية الأخرى فلم يكن كافياً.

وعند دراسة تأثير بعض المواد المحفزة لانطلاق العقار مثل صوديوم لوريل الكبريت, ثنائي ميثيل فورماميد, على قاعدتين دهنية ومائية وجد أن انطلاق العقار يزداد بازدياد تركيز هذة المواد.

اما انطلاق العقار من قواعد هلامية مختلفة فوجد ان أعلى انطلاق من قاعدة الميثيل سيليلوز وأقل انطلاق من قاعدة صوديوم الجينات, وعند اضافة مادة توين٨٠ كمحفز لأنطلاق العقار من قاعدتي ميثيل سيليولوز وهيدروكسي بروبيل ميثيل سيليولوز بتركيزات مختلفة وجد أن ٥% من توين ٨٠ حسن من انطلاق العقار بصورة ملحوظة للقاعدتين , وبإضافة قطرات من مادة ثلاثي ايثانول أمين لنفس القاعدتين السابقتين اعطى انطلاقا كاملاً خلال ١٥٠ دقيقة, وعند تحضير نفس القاعدتين السابقتين في وجود الكحول (هلام كحلي) وجد أن انطلاق العقار كان كاملاً خلال ١٢٠ دقيقة.