Available online on 15.02.2021 at http://ajprd.com

Asian Journal of Pharmaceutical Research and Development

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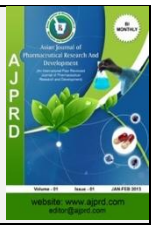

Open Access Research Article

Formulation and Characterization Transdermal Patches of Meloxicam

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A B S T R A C T

Objective: Meloxicam is a non-steroidal anti-inflammatory drug (NSAID), an enolic acid derivative that inhibits the cyclooxygenase-2 (COX-2) enzyme.and is usually used by the oral route in the treatment of a wide variety of rheumatic diseases, including rheumatoid arthritis (RA), osteoarthritis, low back pain and various other joint diseases. However, when given, meloxicam is given orally, causing gastrointestinal side effects such as bleeding, gastric ulcers, nausea and vomiting, which can occur at any time when given orally.

Methods: Transdermal patches of meloxicam were made with a mixture of hydroxypropyl methylcellulose and polyvinylpyrrolidone with various concentrations of enhancers (propylene glycol), that were (F1 10%), (F2 20%), and (F3 30%). Transdermal patches of meloxicam are prepared using the solvent evaporation method. The making of transdermal patches meloxicam was evaluated for various parameters, was evaluated physchochemical, organoleptic, thickness, weight uniformity, folding resistance, moisture content, and swelling properties.

Results: Transdermal patches of meloxicam from three formulas were yellow patches, odorless, slightly wet and flat surface, thickness between 0.0225±0.0005 to 0.0249±0.0001 cm, weight uniformity between 322.56±2.22 to 368.98±1.42 mg, folding resistance between 355.00±3.00 to 386.33±1.53, moisture content between 2.889±0.003 to 3.654±0.009% and swelling between 2.86 up to 3.24%.

Conclusion: The results of the study concluded that the meloxicam transdermal patch preparation had good characteristics, the results obtained met the requirements of a transdermal patch, namely having a flat and slightly wet shape and surface, having uniform weight, thickness, folding resistance and having good patch development power.

Key words: transdermal patch, enhancer variety, physicochemical characteristics, meloxicam

A R T I C L E I N F O: Received; 02 Nov. 2020 Review Complete; 19 Jan. 2021 Accepted; 07 Feb. 2021 Available online 15 Feb. 2021

Cite this article as:

Suhaitamy M, Bangun H, Hasibuan P.A.Z, Formulation and Characterization Transdermal Patches of Meloxicam , Asian Journal of Pharmaceutical Research and Development. 2021; 9(1):38-42. **DOI:** http://dx.doi.org/10.22270/ajprd.v9i1.919

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INTRODUCTION

The use of NSAIDs is an alternative cure for rheumatoid arthritis. One of the drugs used is meloxicam, which works to inhibit the cyclooxygenase-2 (COX-2) enzyme so that this enzyme becomes malfunctioning and is unable to convert arachidonic acid into prostaglandin inflammatory mediators. However, in its administration, meloxicam is given orally, causing gastrointestinal side effects such as bleeding, gastric ulcers, nausea and vomiting, which can occur at any time when given orally (Rajabalaya, et.al, 2008)[8].In general, at least 10 to 20% of patients develop dyspepsia after using this drug. Within the six month period of treatment, 5 to 15% of arthritis patients are thought to discontinue treatment because of dyspepsia. The mortality rate of patients treated for upper gastrointestinal bleeding associated with the use of non-steroidal anti-inflammatory drugs is around 5 to 10% (Azizah L. 2013)[1].To reduce the effect on the gastrointestinal tract, the approach is to make transdermal preparations, that were a delivery system that

utilizes the skin (transdermal) as the entry point for drugs. drug adhesive patch that is placed over the skin to deliver a specific dose of drug through the skin at a predetermined rate of release to reach the bloodstream. In addition to controlling the rate of drug release, this can also improve patient compliance in drug use (Shet, N.S.and Mistry, R.B., 2011)[6].

MATERIALS AND METHODS

Materials

A transdermal patch is defined as a Screw micrometers, analytical scales, magnetic stirrers, ovens, petri dishes, desiccators and glassware. The materials used are Meloksikam, hydroxyl propyl methyl cellulose (HPMC), polyvinyl pyrolidone (PVP), propylene glycol, phosphate buffer saline (PBS), ethanol, dichloromethane.

Preparation *transdermal patch* of Meloxicam

The meloxicam transdermal patch formula is designed according to table 3.1

Table: 1 Formula design

Bahan	Formula		
	F1	F2	F3
Meloksikam	7,5 mg	7,5 mg	7,5 mg
Polivinil pyrolidon (PVP)	146,25 mg	146,25 mg	146,25 mg
hidroksipropil metilselulosa (HPMC)	146,25 mg	146,25 mg	146,25 mg
Propilen glikol	30 mg	60 mg	90 mg
Etanol	5 ml	5 ml	5 ml
Dichloromethana	5 ml	5 ml	5 ml

Preparation of Meloxicam transdermal patches

Transdermal patches are prepared by solvent evaporation (evaporation) techniq ue. Polymers, drugs and plasticizers are dissolved in ethanol: dichloromethane. The solution was mixed in a beaker and stirred slowly for 24 hours with a magnetic stirrer so that the mixture was homogeneous. Then the resulting solution is poured into a petri dish. The solvent was allowed to evaporate at 40 ° C, then patch evaluation was carried out (Munoz M.D., 2017)[3].

Evaluation And Characterization Meloxicam

Organoleptic

Organoleptic observations carried out included color, odor and patch surface (Sharma, et al., 2016).

Thickness

As a uniform film thickness is desired, the film thickness is measured at three different places using a micrometer, and the average value is calculated (Lakhani P., 2015)[2].

Weight uniformity

Five patches were randomly selected and weighed accurately. the mean is calculated. Individual weight should not deviate significantly from the average weight. The difference in patch weight gives an idea of the weight variation (Lakhani P., 2015)[2].

Folding resistance (elasticity)

The folding resistance is the number of creases required to break a polymer patch. This test not only describes the strength of patches prepared using different polymers, but also examines how efficiently the polymer provides flexibility. This test involves the simple phenomenon of repeatedly folding the patch in the same place until it breaks. Thus, it can be seen that the number of patches that can be folded in the same place without breaking / cracking gives a folding resistance value of the patch (Lakhani P., 2015)[2].

Moisture content (water content)

Each patch that has been prepared is weighed (initial weight) and stored in a desiccator containing silica gel for 24 hours. The patches are then weighed again (final weight) (Shabbir, et al., 2017)[4].

$$\text{Moisture content} = \frac{(\text{initial weight} - \text{final weigh})}{\text{initial weight}} \text{ X } 100\%$$

Swelling Test

This test checks for patch development due to the presence of a polymer. This test requires a petri dish and double distilled water, to see how much the patch will expand on contact with water. Patches of 3.14 cm² were weighed and placed in a petri dish containing 10 ml of double distilled water and allowed to absorb within a certain time. The increase in patch weight was then determined at specified time intervals until a constant weight was observed. The degree of swelling (S%) is calculated using the formula

$$S(\%) = \frac{W_t - W_0}{W_0} X\ 100$$

Where, S is the percent swelling, Wt is the weight of the patch at the time of treatment, W0 is the weight of the patch at time zero (Lakhani P., 2015)[2].

RESULTS AND DISCUSSION

Organoleptic

Organoleptic testing is carried out by looking at the color, smell and condition of the resulting patch surface.

This test is carried out by 6 people to ensure the alignment of the results and the condition of the patch organoleptically. Organoleptic observation results can be seen in Table 4.1

Table: 2 Organoleptic Results

Formula	Colors	Odores	Surface consistency and condition
F1	Yellow	Odorless	surface and slightly wet
F2	Yellow	Odorless	surface and slightly wet
F3	Yellow	Odorless	surface and slightly wet

Based on the observations, the patch results from the three formulas were flat and slightly wet.

Thickness Test

The thickness test was carried out to determine the uniformity of the resulting patch thickness, the thickness obtained indicates the uniformity of the patch solution poured on the mold. This test is performed by measuring the patch at five different points using a screw micrometer. Calculated the mean and standard deviation of thickness. The results can be seen in table 4.2

Table: 3 Thickness Results

Formula		Patch Thickness (mg)		Rata-rata ± SD
	Replication 1	Replication 2	Replication 3	
F1	0,0221	0,0231	0,0224	0,0225 ± 0,0005
F2	0,0232	0,0235	0,0234	0,0234 ± 0,0002
F3	0,0248	0,0250	0,0249	0,0249 ± 0,0001

From the results of testing the thickness of the meloxicam transdermal patch preparations, the mean and standard deviation values were 0.0225 ± 0.0005 to 0.0249 ± 0.0001.

Weight Uniformity

Weight testing is carried out to determine the uniformity of the weights of each patch and to ensure that the patches are (Sharma, et al., 2013)[5]. The results can be seen in the table

Table: 4 Weight Results

Formula	Weight (mg)					Rata-rata ± SD
	Patch 1	Patch 2	Patch 3	Patch 4	Patch 5	
F1	321,60	320,10	325,70	323,90	321,50	322,56 ± 2,22
F2	341,20	339,70	338,20	340,40	342,40	340,38 ± 1,58
F3	367,30	370,40	369,30	370,20	367,70	368,98 ±1,42

Based on the results of the weight uniformity test, the average value was between 322.56 ± 2.22 mg to 368.98 ± 1.42. This shows that there is a reduction in the weight of the meloxicam transdermal patch preparation that occurs during the process of making the meloxicam transdermal patch preparation.

Folding resistance (elasticity)

The folding resistance test aims to determine the folding capacity of the polymer patch (Sharma, et al., 2013)[4]. This test can show the ability of the enhancer used, namely propylene glycol and the strength of the patch prepared using several polymers. The results can be seen in table 4.4 below:

Table:5 Crease Resistance Results

Formula		Crease Resistance		Rata-rata ± SD
	Replication 1	Replication 2	Replication 3	
F1	352	358	355	355,00 ± 3,00
F2	368	366	372	368,67 ± 3,00
F3	388	385	386	386,33 ± 3,00

Based on table 4.3, the results of the folding resistance of the three transdermal meloxicam patch preparations were obtained between 355.00 ± 3.00 to 386.33 ± 3.00. folded up to 300 times (Lakhani, et al., 2015)[2].

Moisture Content

Moisture content testing aims to determine the water content in patch preparations which can affect the stability of the preparation. If the water content is too high it can cause contamination of microorganisms so that the stability of the preparation will decrease (Shivaraj, et al., 2010)[7]. The results can be seen in table 4.5 below:

Table: 6 Percent Moisture Content the Transdermal Patch of Meloxicam

	Persen Moisture content			
Formula	Replication 1	Replication 2	Replication 3	Rata-rata ± SD
F1	2,891	2,886	2,890	2,889 ± 0,003
F2	3,455	3,452	3,459	3,455 ± 0,004
F3	3,650	3,648	3,665	3,654 ± 0,009

A patch is said to be good if the patch is dry and has little water content, so that the stability of the patch will be good. The range of water content required is 1 - 10% . Based on table 4.5, the results of the moisture test for the transdermal meloxicam patch preparations obtained the average percent yield between 2.889 ± 0.003% to 3.654 ± 0.009%. This shows that the transdermal patch meloxicam has met the requirements.

Swelling Test

The development test was carried out to determine the bioadhesive properties of the polymer used. The development test was carried out 3 repetitions, the results can be seen in table 4.6 below:

Table: 7 Swelling Results

Waktu	Percent Swelling (%)		
	F1	F2	F3
0	0,00	0,00	0,00
5	1,30	1,52	1,63
10	1,68	1,88	1,92
15	1,93	2,10	2,23
20	2,32	2,47	2,61
25	2,57	2,73	2,86
30	2,86	3,10	3,22

Based on the results of the observation in table 4.6, it is obtained that the percent of the degree of development is F3> F2> F1, this shows that the longer the immersion time will increase the degree of patch development. The use of hygroscopic propylene glycol is able to bind water together with an increase in immersion time (Rowe, et al, 2009)[9].

CONCLUSION

The results of the study concluded that the meloxicam transdermal patch preparations had good characteristics, the results obtained met the requirements of a transdermal patch, namely having a flat and slightly wet shape and surface, having good weight and thickness uniformity, meeting the folding resistance requirements and having good patch development power. good.

ACKNOWLEDMENT

Researchers appreciate thanks to the pharmaceutical department, faculty of pharmacy, University of North Sumateraand PT. Kimia Farma, Indonesia.

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