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FORMULATION AND EVALUATION OF TRANSDERMALPATCHES OF NABUMETONE

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ABSTRACT
In the sector of medical practices, there is a vital impact of Transdermal Drug Delivery System. APrécised quantity of drug is delivered into the blood stream through the skin and it is delivered by the medicated patches. The Transdermal Drug Delivery having a merit over the other conventional system of drug delivery is that the drug is released in sustained form from the patches into the patients, and usually the drug the drug is released in control manner either from body heat melting thin layers of drug embedded in the adhesive or the drug is released from a reservoir covered by aporous membrane. Then main objective of the recent study is to prepare a transdermal patch of non-steroidal anti-inflammatory drug, Nabumetone using mercury substrate method and the physiochemical parameters were evaluated, the parameters such as weight variation, thickness, moisture uptake, moisture content, drug content, and folding endurance. There are total six transdermal patches were formulated by changing the concentration of ethyl cellulose.

KEYWORDS: Transdermal patches, NSAIDs, Ethyl cellulose, Nabumetone, Skin, Inflammation, Permeation.

INTRODUCTION
Now a days, For systemic therapy or for the local cure and management of tissues beneath the skincan be done with the help of Transdermal Patch, a type of topical delivery of drugs to the healthyundamaged skin. There are various merits of transdermal patches over the other predictable dosage form or controlled release oral system. The transdermal patches facilitates so many things such as avoid dose dumbing, provides constant blood level, increased patient conformity, avoid first pass metabolism.[1,2]

When the drug is applied through the skin, it gives a better option for slow and more controlled pathways for release of drug into the systemic circulation, and by pass "first pass metabolism". There are so many benefits of transdermal patches such as, multiple dosing can be avoided, the patient will be able to apply the transdermal patch, by themselves and they can easily remove it too, the drug level can be maintained for a prolonged time.[3,4]

The patient conformity can be enhanced by using Transdermal drug delivery system, it can prevents so many things such as, the hepatic first pass metabolism can be avoided and other side effects can also be reduced in comparison of other Drug delivery system.[5] When the drug were delivered with the help of Transdermal patch system, it is slow, and the drug release and absorptionwere be controlled. There is no difference due to the over time the plasma drug concentration. In the developing market, there is a lot of demand of Transdermal drug delivery system, that will make a great success in the few upcoming years with the development of new drug delivery systemand new inventions.[6]

There are so many things in oral route of administration, and to overcome that problems, Transdermal Drug Delivery System play a vital role, such as in terms of long term therapy it enhance the patient conformity, sustained drug delivery, avoiding first pass metabolism to reduce the minimizing inter and intra patient in consistency, to maintain drug level in plasma for prolonged time which consistency, and help to avoid treatment when it is important.[7,8]

Characterized by symmetrical circulation, there is a chronic inflammatory disorder, caused by the immune system confronting joints, known as rheumatoid arthritis

(RA).[9]

Long term synovitis strikes the cartilage articularis, leading to joint abnormalities and physiology disorder, strikes the muscle tendon and muscle ligament. For the treatment musculo- skeleton disorders such as rheumatoid arthritis and osteoarthritis, Non-steroidal anti-inflammatory drug arewidely used.[10]

For reducing pain and inflammation, most of the time the Non-steroidal anti-inflammatory drugs (NSAIDS) were formulated in the form of transdermal patches. The Transdermal patches of non-steroidal anti- inflammatory drugs are innocuous and more suitable than oral form of NSAID. There are various types of NSAID tablets were given to the patient with Rheumatism. The Transdermal patches can be helpful for avoiding the adverse effects like high acidity, bleeding ofstomach, ulcers, etc. On the area of damage, strain or twist, the analgesic patch of Non-steroidal anti- inflammatory drug were applied.

When the Transdermal patch smeared topically, the drug penetrate the skin, muscles, sub- cutaneous fatty tissue, the local therapeutic effect produced in adequate amount without touching the higher plasma drug concentrations.[11,12]

Nabumetone

Nabumetone is a non-steroidal anti-inflammatory drug (NSAID) Used in the treatment of Rheumatoid arthritis and osteoarthritis. The Smithkline Beecham were first who developed the trade name of Nabumetone as Relafen and its gets its first approval in December, 1991 by FDA. It is a 6-MNA active metabolite, which is the inhibitor of COX-1 and COX-2. The conversion of arachidonic acid to thrombonane (TXA_2) and Prostaglandin (PGs) is reduced by the inhibition of COX-1 and COX-2.[13]

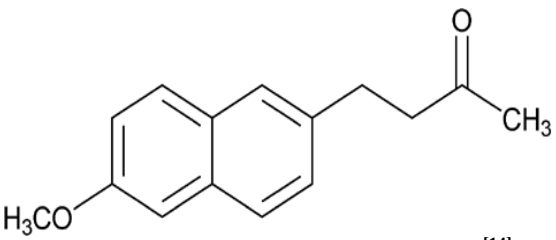


Fig. 1: Structure of nabumetone.[14]

MATERIAL AND METHOD

Chemical required

All the ingredients used in this study were of standard pharmaceutical ranking. Nabumetonewere obtained from the Sigma Aldrich, Merck India. Ethyl Cellulose, Dibutylphthalate, Polyethylene Glycol (PEG-400), Chloroform, Methanol, Cotran^{TM}9720, Microporous Polyethylene Membrane, Acrylic Adhesives were obtained from SHEAT College of Pharmacy and of analytical reagent ranking.

Apparatus required

The apparatus which are needed for making patch Beaker, Glass rod, measuring cylinder, Butter paper, Weighing Balance, Spatula, Petri Dish, Funnel.

Procedure

- The chloroform: methanol solvent (1:4) ratio were made and used as working a working solution.
- The working solution pH were be estimated.
- The polyethylene glycol (PEG 400), ethyl cellulose were dissolved in the working solution.
- The solution were mixed and kept at a side, until, we obtained a clear solution.
- The drug (Nabumetone) were dispersed uniformly in the viscous solution, until, we obtained a clear solution.
- Now the uniform solution were transferred in the petridish.
- The petridish were lubricated with the help of glycerin and the uniform solution in the petridish were dried for 24 hours at room temperature.
- To prevent the fast evaporation of the solvent, the petridish were covered with an invertedfunnel.
- The transdermal patch were completely obtained after 24 hours, by steady lifting from the petridish.
- The transdermal patches were cut into radius of $4cm^2$.[15]

Fig. 1: Nabumetone drug.

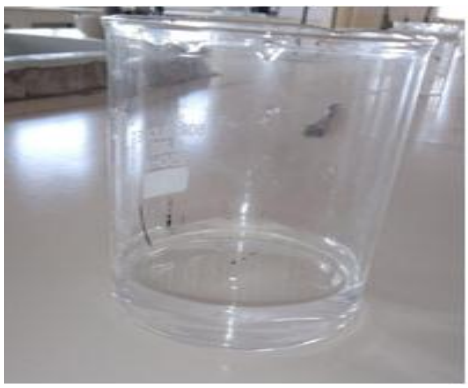


Fig. 2: Working solution. Fig. 3: Patch solution in petridish. Fig. 4: Petri dish is covered with inverted funnel.

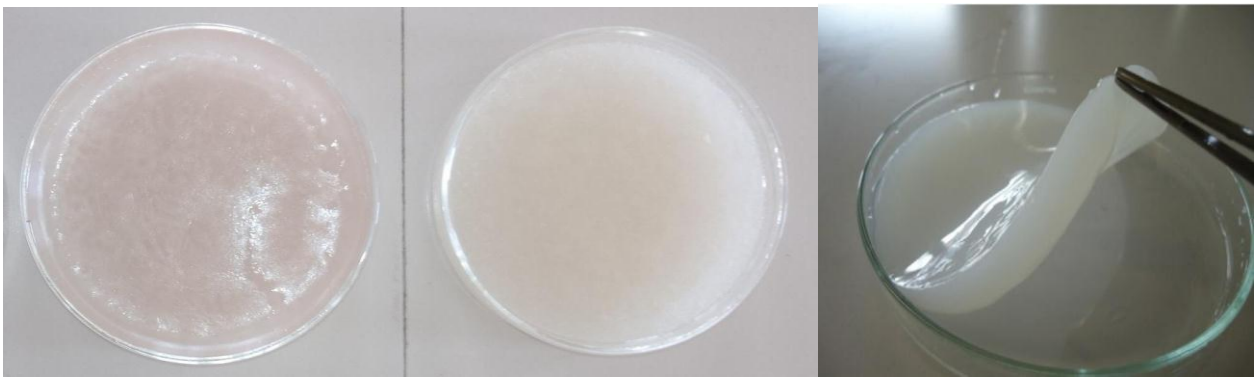


Fig. 5: Patches after 24 hours.

Fig. 6: Transdermal patch of nabumetone.

Table 1: Formulation composition of nabumetone transdermal patches.

Ingredients	F1	F2	F3	F4	F5	F6
Nabumetone(mg)	100	100	100	100	100	100
Ethyl Cellulose (mg)	200	250	300	350	400	450
PEG-400 (ml)	3	3	3	3	3	3
Dibutyl phthalate (ml)	3	3	3	3	3	3
Chloroform: Methanol	1:4	1:4	1:4	1:4	1:4	1:4

Evaluation and Characterization

Thickness of patch

By using thickness gauge and patch, the thickness of patch were estimated at three different- different points. The specific area of the transdermal patch were cut and weighed.[14] A hundred ml volumetric flask were taken filled with phosphate buffer and pieces which were cut, transferred in to it. The volumetric flask were sonicated for atleast 8 hours and the concentration of the solutions were found in approximately nm.[16]

Weight uniformity

By weighing few patches (randomly selected patches), the weight uniformity were estimated. The standard deviation and average weight of patch were determined and calculated. We have to takecare that, the weight of a single patch, should not have a vast difference from the average weight of patch.[17]

Folding endurance

For the formulated patches, the folding endurance were calculated individually. The folding endurance can be defined, as how many times the patch is folded at the similar place to evaluate, either the patch were developed with visible cracks or the patch is break. The number of folds of patch at the similar patch without crack, estimate the value of folding endurance.[18]

Percentage moisture content

Weighed the patch accurately, place that patch in a dessicator for 24 hours with fused calcium chloride and reweighed it, by this, the moisture content of a transdermal patch can be calculated . The following equation were used to calculate the percentage of moisture content of the patch-[19]

Moisture content (%) = Initial mass – final mass / initial mass × 100

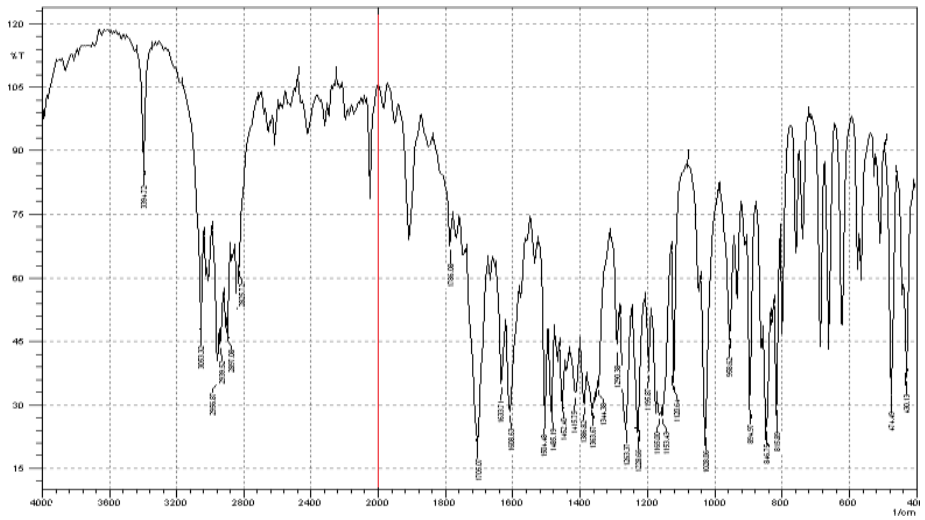
Drug content

The transdermal patches of specific area were dispersed in dichloromethane solution of 5 ml and the required volume of solution were made up to 10ml by adding phosphate buffer of ph 7.4. By using a Rotatory Evaporator at 45℃, the dichloromethane solution were evaporated. For treating a drug-free patch in the same way, the blank solution were prepared. A 0.45 µm membrane were taken to filter the solutions. The solution were diluted and absorbance were read at 274 nm by using a double beam UV-visible spectro-photometer.[20]

RESULT AND DISCUSSION

The FTIR Nabumetone were performed and interpretation were noted in the below mentioned figure. The various parameters were evaluated such as, thickness, weight uniformity, folding endurance, percentage moisture content and drug content of the Nabumetone Transdermal Patch. From the above discussion on this research paper, we can conclude that, all formulations shows good physiochemical properities like thickness, weight uniformity, folding endurance, percentagemoisture, content and drug content of patch.

FTIR Spectra of Nabumetone



Interpretation of FTIR Spectra of Nabumetone

Functional Groups	Actual IR Range	Observed IR Range of Nabumetone
C-H Stretching	2970-2850	2939.54-2897.06
C=O Carbonyl group	1750-1705	1786.10-1705.05
Ether O-CH3	2850–2815	2825.9
C=C-C Aromatic ring stretching	1680-1620	1633.10-1608.61

Table 2: Thickness of nabumetone transdermal patches.

S. No.	Formulation code (F)	Thickness
1	F1	158 ± 5.52
2	F2	160±5.65
3	F3	170±5.60
4	F4	178 ±2.40
5	F5	270±2.83
6	F6	352±4.82

Table 3: Weight uniformity of nabumetone transdermal patches.

S. No.	Formulation code (F)	Weight Uniformity
1	F1	12.52±0.35
2	F2	10.80±0.30
3	F3	15.16±0.50
4	F4	14.95±0.45
5	F5	13.61±0.30
6	F6	15.18±0.45

Table 4: Folding endurance of nabumetone transdermal patches.

S. No.	Formulation code (F)	Folding Endurance
1	F1	210 ± 6.29
2	F2	215±6.40
3	F3	235±7.06
4	F4	240±7.36
5	F5	236±7.15
6	F6	245±7.30

Table 5: Percentage moisture content of nabumetone transdermal patches.

S. No.	Formulation code(F)	Percentage Moisture Content(%)
1	F1	2.30 ± 0.55
2	F2	4.01±0.80
3	F3	2.90±0.60
4	F4	1.95±0.36
5	F5	1.76±0.30
6	F6	1.62±0.32

Table 6: Drug content of nabumetone transdermal patches.

S. No.	Formulation code (F)	Drug Content(%)
1	F1	97.6 ± 2.45
2	F2	98.5±2.46
3	F3	96.8±2.36
4	F4	95.5±2.30
5	F5	98.6 ±2.50
6	F6	99.9±2.48

CONCLUSION

The Transdermal patches of Nabumetone were formulated successfully by taking different concentrations of ethyl cellulose by solvent casting method. We have concluded from the present work that, as the concentration of polymer increases a thickness of

the Nabumetone Transdermal patch, weight uniformity and folding endurance enhances the percentage moisture content and percentage moisture uptake reduced with enhance concentration of polymer.

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