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The Role of Transdermal Drugs in the Treatment of chronic diseases

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Abstract: Treatments of acute and chronic diseases have been accomplished by delivery of drugs to patients using various pharmaceutical dosage forms. These dosage forms are known to provide a prompt release of drug. But recently several technical advancements have been done and resulted in new techniques for drug delivery. These techniques are capable of controlling the rate of drug release.In this work an attempt was made to formulate and evaluate TDDS for sustained release Granisetron Hcl by solvent casting method. Low molecular weight, good permeability and shorter half-life of Granisetron Hcl made it a suitable drug candidate for the development of transdermal patches.The main objective of formulating the transdermal system was to prolong the drug release time, reduce the frequency of administration and to improve patient compliance. The compatibility parameters characterization was done by DSC and IR method.

Key Words: chronic, pharmaceutical, TDDS (Transdermal drug delivery System)

INTRODUCTION: Treatments of acute and chronic diseases have been accomplished by delivery of drugs to patients using various pharmaceutical dosage forms. These dosage forms are known to provide a prompt release of drug. But recently several technical advancements have been done and resulted in new techniques for drug delivery. These techniques are capable of controlling the rate of drug release.

The term-*controlled release* has a meaning that goes beyond scope of sustained release. The release of drug ingredients from a controlled release drug delivery advances at a rate profile that is not only predictable kinetically, but also reproducible from one unit to another.

Controlled release denotes that the system is able to provide some actual therapeutic control whether this temporal nature, spatial nature or both. In other words, the systems attempts to control drug concentration in the target tissues. Sustained release dosage forms, repetitive, intermittent dosing of a drug occurs from one or more immediate- release units incorporated into a single dosage form.

The term "Transdermal Drug Delivery" (TDD) essentially means any type of a substrate or formulation containing substances that allows the drug to transit from the outside of the skin through various skin layers and finally into the systemic circulation to produce a pharmacological action. Historically, developments in TDD have been incremental and there is increased recognition that the skin can also serve as a port for administration for systemically active drugs.

Results and Discussion:

Evaluations of Patches

Physical evaluations

1. Thickness

The thickness ranged between 0.090 to 0.110 mm. The values obtained for all the formulations are given in the table 1 and 2.

2. Tensile Strength

The tensile strength results indicate the strength of film and the risk of film cracking. But, no sign of cracking in prepared transdermal films was observed, which might be attributed to the addition of the plasticizer, propylene glycol. The Tensile Strength ranged between 9.50 to 12.00 Kg/mm^2. The results of tensile strength are shown in table 1 and 2.

3. Percentage Elongation

The % elongation was found to be in the range of 59.00 to 65.00 %. The results obtained for all the formulations are tabulated in the table 1and 2.

4. Folding endurance

The folding endurance measures the ability of patch to withstand rupture. The folding endurance was measured manually and results indicated that the patches would not break and would maintain their integrity with general skin folding when used. The folding endurance was found to be in the range of 251to 270. The values for all fourteen formulations are given in the table 1 and 2. This data revealed that the patches had good mechanical strength along with flexibility.

5. Weight Variation Study

The weights ranged between 169 to 176 mg which indicated that different batches of patch weights were relatively similar. The values for all the formulations are tabulated in the table 1 and 2.

Table 1: Thickness, Tensile Strength, Percentage Elongation, Folding Endurance and weight of Optimized Granisetron Hcl patches using combinations of HPMC E15 and Eudragit RL 100 in various rations

Sr. No.	Batch Code	Thickness (mm)	Tensile Strength Kg/mm^2	Percentage Elongation	Folding endurance	Weight in mg
1	G-1	0.096 ± 0.0041	11.0147 ± 0.5946	62.5% ± 1.0937%	257 ± 3.6831	172.484 ± 3.06562
2	G-2	0.098 ± 0.0055	10.08 ± 0.7732	61.2245% ± 1.4786%	253 ± 5.2781	175.375 ± 3.3349
3	G-3	0.104 ± 0.0073	10.4313 ± 0.4739	60.0961% ± 1.9506%	263 ± 4.9801	169.247 ± 3.2965

*Values expressed as Mean± SD; n=3

6. Flatness Study

An idyllic patch should be formulated in such a way that it possesses a smooth surface and it should not constrict with time. Flatness studies were performed to judge the same. The result of flatness and thickness shown in table given below and low value of standard deviation indicates good uniformity. The results of the flatness study showed that none of the formulations had many differences in the strip lengths before and after their cuts indicating good uniformity of the polymers throughout the transdermal films. It indicates much closed to 100% flatness observed in the formulated patches. Thus, very minute amount of constriction was observed in the film of any formulation and it indicates smooth flat surface of the patches and these formulations can maintain uniform surface when they are applied onto skin.

7. Percentage Moisture Content

The physicochemical studies like moisture content and moisture uptake provide the information regarding the stability of the formulation. The moisture content was determined by keeping the drug matrix patches in a desiccator containing activated silica until they showed constant weight. The percentage moisture content was calculated from the weight differences relative to the final weight. The results of the moisture content studies for different formulations are shown in table given below. The moisture content varied to a small extent in all fourteen batches. However, there was an increase in the moisture content with an increase in the hydrophilic polymer, HPMC in matrix transdermal patches. The moisture content of the prepared transdermal film was low, which could help the formulations remain stable and from being a completely dried and reduce brittleness during storage.

10. Drug Content

Good uniformity of drug content among the batches was observed with all formulations and ranged from 98.89% to 100.23%. The results indicate that the process employed to prepare patches in this study was capable of producing patches with uniform drug content and minimal patch variability.

Table 2: Flatness, % Moisture Content and % Drug Content of Optimized Granisetron Hcl patches using combinations of HPMC E15 and Eudragit RL 100 in various rations

Sr. No.	Batch Code	Flatness	% Moisture Content	% Drug Content
1	G-1	100% ± 0.0132	6.6352% ± 0.2086%	99.47% ± 0.2636%
2	G-2	100% ± 0.0102	5.3715% ± 0.1984%	99.32% ± 0.4305%
3	G-3	100% ± 0.0121	4.88% ± 0.2853%	99.87% ± 0.3529%

*Values expressed as Mean± SD; n=3

8. Percentage Moisture Uptake

The percentage moisture uptake was calculated from the weight difference relative to the initial weight after exposing the prepared patches to relative humidity. The results of moisture uptake studies for different formulations are shown in table 3 and 4. The percentage moisture uptake was also found to increase with increasing concentration of hydrophilic polymer, HPMC and percentage increase in humidity. The moisture uptake of the transdermal formulations was also low, which could protect the formulations from microbial contamination and also reduce bulkiness of films.

Table 3: % Moisture Uptake at (RH 60 % ± 5%), (RH 75 % ± 5%) and (RH 90 % ± 5%) of Optimized Granisetron Hcl patches using combinations of HPMC E15 and Eudragit RL 100 in various rations

Sr. No.	Batch Code	% Moisture Uptake (RH 60 % ± 5%)	% Moisture Uptake (RH 75 % ± 5%)	% Moisture Uptake (RH 90 % ± 5%)
1	G-1	2.301% ± 0.1329%	4.6161% ± 0.1137%	7.1227% ± 0.1602
2	G-2	2.0056% ± 0.1038%	4.2096% ± 0.1028%	6.5295% ± 0.1396%
3	G-3	1.7564% ± 0.1282%	3.8649% ± 0.1302%	6.1074% ± 0.1407%

*Values expressed as Mean± SD; n=3

Table 4: % Moisture Uptake at (RH 60 % ± 5%), (RH 75 % ± 5%) and (RH 90 % ± 5%) of Optimized Granisetron Hcl patches using combinations of HPMC E15 and Eudragit RS 100 in various rations

***Values expressed as Mean± SD; n=3**

9. Water Vapour Transmission Rate (WVTR)

The Water Vapour Transmission Rate was calculated from the weight difference relative to the initial weight after exposing the prepared patches placed over the brim of transmission cell to relative humidity. The results of Water Vapour Transmission Rate studies for different formulations are shown in Table 5. The Water Vapour Transmission Rate was also found to increase with increasing concentration of hydrophilic polymer, HPMC which might be attributed to the hydrophilic nature of the HPMC and also increase with percentage increase in humidity.

Table 5: Water Vapour Transmission Rate at (RH 60 % ± 5%), (RH 75 % ± 5%) and (RH 90 % ± 5%) of Optimized Granisetron Hcl patches using combinations of HPMC E15 and Eudragit RL 100 in various rations

Sr. No.	Batch Code	WVTR (RH 60 % ± 5%)	WVTR (RH 75 % ± 5%)	WVTR (RH 90 % ± 5%)
1	G-1	0.1594% ± 0.0251%	0.2705% ± 0.0328%	0.5305% ± 0.0364%
2	G-2	0.1527% ± 0.0473%	0.2642% ± 0.0293%	0.5072% ± 0.0452%
3	G-3	0.1467% ± 0.0519%	0.2341% ± 0.0429%	0.4835% ± 0.0473%

*Values expressed as Mean± SD; n=3

Summary:

In this work an attempt was made to formulate and evaluate TDDS for sustained release Granisetron Hcl by solvent casting method. Low molecular weight, good permeability and shorter half-life of Granisetron Hcl made it a suitable drug candidate for the development of transdermal patches.

The main objective of formulating the transdermal system was to prolong the drug release time, reduce the frequency of administration and to improve patient compliance. The compatibility parameters characterization was done by DSC and IR method.

Fourteen formulations were prepared using different polymers in different ratios and combinations, along with plasticizers and penetration enhancer. Mercury was used as a substrate for pouring the polymeric solution.

The films were evaluated for thickness, tensile strength, percent elongation, weight variation study, folding endurance, flatness study, percentage moisture content, percentage moisture uptake, water vapour transmission rate, drug content, *in vitro* and *ex-vivo* diffusion studies using Keshary Chein diffusion cell.

Conclusion: Nausea and vomiting are among the most distressing side effects associated with chemotherapy for cancer treatment. Administration of an combination of antiemetic drugs of different classes simultaneously from a single transdermal therapeutic system can potentially increase the confidence in cares and treatment of the patients, who already are frayed of the needles and injections frequently used in chemotherapy .

Optimized patches were subjected to various evaluation parameters like thickness, tensile strength, percent elongation, weight variation study, folding endurance, flatness study, percentage moisture content, percentage moisture uptake, water vapour transmission rate, drug content, permeation study.

In the future study of the present work assessment of in vivo behaviour of transdermal matrix patches of Granisetron Hcl should be performed. In vitro In vivo assessment study should also be performed. Also other film forming polymers like chitosan, xanthan gum, sodium alginate and polyvinyl pyrrolidone K30D will be studied for determining their effects on permeation profile. Various penetration enhancers will also be studied for their effect on release mechanism. Various plasticizers will also be studied to determine their effects on tensile strength, percentage elongation and folding endurance of patch.

References:

1. Y.W. Chien. "Novel Drug Delivery Systems", 2nd Edition, Drugs and Pharmaceutical Sciences, Volume-50, Marcel Dekker, Inc. pp 301-370.
2. B. C. Finnin and T. M. Morgan. Transdermal Penetration. J Pharm Sci. **88**(10) pp 955-958; *1999*.
3. "European Pharmacopoeia" 6.0, 5th Edition,Volume-1,pp737; *2008.*
4. L. V. Allen, N. G. Popovich and H. C. Ansel. Ansel's Pharmaceutical Dosage Forms and Drug Delivery Systems, 8th Edition, Lippincott Williams & Wilkins, pp 298-315; *2005*.
5. B. Barry. Transdermal Drug Delivery. In Ed: M. E. Aulton, Pharmaceutics: The Science of Dosage Form Design, Churchill Livingston. pp 499-533; *2002*.
6. K. Garala, N. Faldu, B. Basu, R. Bhalodia, K. Mehta and B. Joshi.Chemical Penetration Enhancement: A Review. J Pharm Research. **2**(12); pp 1804-1808; *2009*.
7. S. P. Vyas and R. K. Khar. Controlled Drug Delivery: Concepts and Advances, VallabhPrakashan, 1st Edition. pp 411-447; *2002*.
8. B. Wang, T. Siahaan and R. A. Soltero. Drug Delivery: Principles and Applications, John Wiley & Sons. pp 69; *2005.*
9. T. Selzer, P. Botsem, H. Kindel and G. Hoffman. Transdermal therapeutic system for the delivery of Lerisetron. US Patent 01/74338 A1; *2001*.
10. J. B. Franz. Composition for the transdermal delivery of Lerisetron. US Patent 006136807A; *2000.*