

Health care practitioners' perceptions of transdermal therapeutic systems in Palestinian territories

Zaid Abdel Naser

Department of Chemistry and Pharmaceutical Technology, College of Pharmacy, An-Najah National University - 7, Nablus, Palestine

To evaluate the scientific knowledge and attitudes of health professionals in Palestine regarding the advantages of transdermal therapeutic systems (TTSs) over conventional therapy. Data were gathered from a questionnaire that was handed out to community pharmacists and physicians. Pharmaceutical industry decision makers were enrolled in this study. Data were analyzed using the SPSS statistical software program version 10. 79.5% of pharmacists and 74% of physicians thought that TTSs eliminate variables due to gut absorption. 78.8% of pharmacists and 65.6% of physicians were in agreement regarding the capacity of TTSs to avoid first-pass metabolism. In this study, 83.3% of the physicians and 81.3% pharmacists still agree that TTSs may provide controlled release. 55.8% of pharmacists and only 26% of physicians believed that TTSs eliminate drug-plasma fluctuation. 56.8% of pharmacists and 63.5% of physicians agreed that TTSs can use drugs with low therapeutic indices. 81.3% of pharmacists and 85.4% of physicians believed that TTSs are not invasive and can be removed easily to stop drug administration. 81.3% of physicians and 89.1% of pharmacists thought that TTSs may irritate or sensitize the skin. Eighty-four percent of pharmacists and 75% of physicians recognize that TTSs should contain drugs that must be stable and have correct physicochemical properties. The importance of TTSs is understood and appreciated by Palestinian health personnel. Pharmaceutical industries should pay more attention to the development and production of TTSs due to the valuable advantages of this therapeutic system.

Key words: *Transdermal therapeutic system, ease of application, compliance, safety*

INTRODUCTION

There has been an increased interest in drug administration via the skin for both local therapeutic effects on diseased skin (topical delivery) as well as for systemic delivery (transdermal delivery) of drugs. The skin as a route for systemic drug administration has become very attractive since the introduction of transdermal therapeutic systems (TTSs) in the form of patches. These fascinating therapeutic delivery systems have gained further importance and so they have been increasingly used in the past two decades.^[1-8] In fact, TTSs offer many advantages over conventional therapy, such as:

(i) Eliminating variables due to gut absorption and minimizing inter- and inpatient variability,^[9]

- (ii) Bypassing first-pass metabolism,^[10,11]
- (iii) Providing controlled release, which improves patient compliance,^[12,13]
- (iv) Maintaining a constant, prolonged drug concentration and eliminating drug-plasma fluctuation,^[14]
- (v) Making it non-invasive and safe because the therapy can be quickly terminated by simple removal of the system from the skin surface,^[12]
- (vi) This makes possible the delivery of drugs with a low therapeutic index in TTS preparations.^[3,5] Unfortunately, only relatively potent drugs that possess suitable physico-chemical characteristics of the drug, such as molecular weight, three-dimensional structure and partition coefficient and good stability are suitable candidates for TTSs.^[15-19] Other factors such as skin irritation and sensitization among users also were the main inconvenience of these systems.^[20-23] Despite these inconveniences, the improvement of patient compliance in long-term therapy encouraged many pharmaceutical companies to develop a TTS for many active ingredients. In fact, since the first approved transdermal patch of scopolamine, there have been

Address for correspondence:

Dr. Zaid Abdel Naser, Associate Professor, Department of Chemistry and Pharmaceutical Technology, College of Pharmacy, An-Najah National University - 7, Nablus, Palestine. E-mail: da1_naser@yahoo.com

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several financially successful passive transdermal drug delivery patches-including those of nicotine, testosterone nitroglycerin, estradiol, clonidine and fentanyl.^[3,5-7,24] This commercial success has generated further interest to expand the range of therapeutics for the transdermal route. In the light of what was mentioned above about this therapeutic system, we decided to evaluate the attitudes of Palestinian health professionals and their assessment toward the advantages and disadvantages of TTSs in the pharmaceutical field.

MATERIALS AND METHODS

This study was based on a questionnaire that was composed of two sections. The first part was a Table where health professionals were asked to fill in details with trade names of TTS products present in the Palestinian market, their manufacturing companies and the active ingredients contained therein. The second part was also a Table where the health professionals were asked to comment on a statement regarding the advantages of TTS as a therapeutic system such as bypassing the first-pass metabolism, giving controlled release, maintaining a constant and prolonged plasma concentration and stopping the administration of the drug at any moment. Health professionals were also asked about the disadvantages of TTSs, such as irritation and sensitization, and the limitation of this therapeutic system to only those drugs with appropriate physicochemical properties. The questionnaire was handed out during the period of 15th of October till 15th November, 2008. The questionnaire was distributed to both physicians and community pharmacists by the fourth year pharmacy students of An-Najah University. After collection of the filled forms, the data were entered and descriptively analyzed using statistical software program version 10 (SPSS), (SPSS Inc., Chicago, IL, USA).

RESULTS

Physicians' and pharmacists' attitudes

The questionnaire was distributed throughout the cities of the west bank where it was filled by 104 physicians and 156 community pharmacists. In addition, 18 (16) decision makers also responded by filling the specified part of the questionnaire. Only seven (7) different trade names were found in the Palestinian market, three of which were nicotine TTS patches, two were nitroglycerin, one was fentanyl TTS patch while the remaining one was ethinylestradiol and norelgestromin TTs patch. None of these patches was produced locally [Table 1].

Among the participant pharmacists, 79.5 and 74% of the physicians thought that TTSs eliminate variables due to gut absorption. The results obtained also showed that the majority of community pharmacists (78.8%) and most physicians (65.6%) were in agreement regarding the capacity of TTSs to avoid the first-pass metabolism [Table 2]. In

this study, the majority of the physicians and pharmacists (83.3 and 81.3%) agreed that TTSs may provide controlled release, which improves patient compliance better than the corresponding other dosage forms containing the same drug [Table 2]. About half of the community pharmacists (55.4%) believed that TTSs eliminate drug-plasma fluctuation while only 26% of the physicians had the same belief. As for the use of drugs with a low therapeutic index, about half (56.8%) of the community pharmacists agreed that TTSs can use drugs with a low therapeutic index while 63.5% of the physicians agreed with this point [Table 2]. Almost equal numbers of pharmacists and physicians had the same opinions regarding the non-invasivity and higher safety of TTSs compared with other dosage forms such as oral, rectal and parenteral, with 81.4% of the community pharmacists believing that TTSs are not invasive and can be removed easily to stop drug administration while 85.4% of physicians had the same thought. On the other hand, 81.3% of the physicians thought that TTSs may irritate or sensitize the skin and, as per the highest majority of the pharmacists, 89.1% had the same thought [Table 2]. As for the final statement of "TTSs should contain drugs that must be stable and have correct physicochemical properties," different results were obtained from pharmacists and physicians. In fact, about 84% of community pharmacists and 75% of physicians who participated recognized that TTSs should contain drugs that must be stable and have correct physicochemical properties [Table 2].

Industrial personnel viewpoints

Here, industrial personnel were asked to pick the reasons why their pharmaceutical companies are not developing TTSs [Table 3]. All industrial personnel reported that their companies have never developed TTS in the past. About 64.3% of pharmaceutical decision makers thought that the reason behind the non-development of these therapeutic systems was lack of technology or specialized personnel to develop this TTS. A high percentage of the questioned personnel (78.6%) believed that poor development of this therapeutic system may be due to either strategic company decisions or to the bad understanding of health professionals regarding the

Table 1: Transdermal therapeutic systems available in the Palestinian pharmaceutical market

Trade name	Pharmaceutically active ingredient	Manufacturer
Nicotinell TTS	Nicotine	Novartis
Niquitin cq	Nicotine	Glaxo-Smithkline
Nicorette patch	Nicotine	Pharmacia and Upjohn
Nitroderm TTS	Nitroglycerin	Novartis
Deponit TTS	Nitroglycerin	Schwarz-Pharma
Evra transdemal patch	Ethinylestradiol and norelgestromin	Janssen-Cilag
Durogesic TTS patch	Fentanyl	Janssen-Cilag

Table 2: The comments of physicians and pharmacists regarding the advantages and disadvantages of transdermal therapeutic systems

Statements asked to physicians and pharmacists regarding the characteristics of TTS	Pharmacists			Physicians		
	Agree	Disagree	Uncertain	Agree	Disagree	Uncertain
TTSs eliminate variables due to gut absorption and minimizing inter- and inpatient variability	79.5	15.4	5.1	74	18.8	7.2
TTSs eliminate first-pass metabolism	78.8	17.3	3.8	65.6	10.4	24
TTSs provide controlled release, which improves patient compliance	83.3	13.5	3.2	81.3	13.5	5.2
TTSs maintain a constant and prolonged eliminating drug-plasma fluctuation	55.4	28.8	14.8	26	58.4	15.6
TTSs may contain drugs with a low therapeutic index	56.8	27.7	15.5	63.5	22.9	13.5
TTSs are safe and not invasive because it is possible to interrupt treatment when necessary	81.4	13.5	5.1	85.4	8.3	6.3
Only relatively potent drugs that possess suitable physico-chemical characteristics are suitable candidates for TTSs production	84	9	7	75	12.5	11.5
TTSs may cause skin irritation and sensitization among users	89.1	5.1	5.8	81.3	4.2	14.6

Table 3: The comments of industrial personnel regarding the reasons of poor development of transdermal therapeutic systems. The total number of industrial personnel was 18

Statements asked to industrial personnel regarding the reason of not developing chewable tablets	Agree (%)	Disagree (%)	Uncertain (%)
Very costly	42.9	21.4	35.7
Lack of technology or specialized personnel	64.3	21.4	14.3
TTSs are not fully evaluated and accepted by physicians and pharmacists	71.4	14.3	14.3
The company has more important strategies	78.6	7.1	14.3

importance of TTS in the therapeutic field (71.4%). Only 42.9% of the interviewed decision makers believed that high cost of production relies on the strategy of non-developing TTS.

DISCUSSION

The number of TTS formulations found in the Palestinian market shows that this therapeutic system is poorly available in this country. The majority of the participating pharmacists and physicians had nearly positive opinions about what was expected regarding the advantages and disadvantages of TTSs. This result should encourage the success of these therapeutic systems in the Palestinian pharmaceutical market and thus improve the success opportunities of the therapeutic treatment since the mentioned advantages should play a fundamental role in the improvement of drug compliance. In fact, the non-invasivity of these systems in comparison with parenteral formulations is a very important factor in the selection of therapy where TTSs play an important role in order to avoid pain and suffering due to the use of a syringe,

especially in the treatment of some chronic diseases. Regarding the capacity of TTSs in eliminating drug-plasma fluctuation, 55.8% of the pharmacists and only 26% of the physicians agreed with this point. These different results may be expected because the pharmacists' background studies include a better understanding of the issues of the bioavailability of pharmaceutical dosage forms. With this advantage more understood by pharmacists, it is expected that a preferential attitude toward these therapeutic systems is practiced when supplying certain medications in community pharmacies, especially when it comes to non-prescription drugs. On the other hand, the fact that only 26% of the physicians knew this fact may have a negative effect on the number of TTS prescribed, which may be one of the reasons behind the poor consideration of these therapeutic systems among physicians. Another very important result to be discussed is the use of drugs with low therapeutic indices where, unfortunately, only about half of the pharmacists but most physicians (63.5%) agreed with this issue. In fact, many problems in dose precision arise when liquid dosage forms contain drugs with low therapeutic indices, especially in pediatric patients.^[5-7] Therefore, the use of TTSs containing these drugs should resolve their dose precision. Concerning the results related to the ease of application and removing of patch to stop drug administration resulting in higher safety shows that the majority of pharmacists and physicians agreed with this. In fact, TTSs are considered not only as a safe mode of drug administration but also as an easy method of administration of drugs with bad organoleptic properties without the need of uses of injectable or rectal routes, which usually have bad patient compliance. In fact, the ease of administration of medications to children presents a challenge for both health professionals and patients equally. For many adults, it is not always easy to swallow many drugs in the form of tablets. In fact, a study performed in Norway showed that every third woman and every sixth

man agreed to have problems with swallowing tablets.^[1] Thus, for another time, the ease of administration of drugs such as TTSs can solve these inconveniences. Concerning the results of the questionnaire given to decision makers in the pharmaceutical industry, it was interesting to see that this category has recognized precisely three reasons for the non-development of TTSs. In fact, 64.3% of them said that lack of technology or specialized personnel is the obstacle. 71.4% said that the reason is that this therapeutic system is not completely understood and accepted by pharmacists and physicians, while 78.6% said that more important strategies of the company lie under the non-development of this therapeutic system. However, the first reason can be solved by well-organized scientific cooperation between universities and the pharmaceutical industry, as is the case in many industrial countries, whereby the expertise of university professors can be of great help in this field. The second reason should not be absolutely a serious problem, since the first part of this study shows that the majority of interviewed pharmacists and physicians have a positive idea about the many advantages of TTSs. However, a well-organized labor of medical representatives who must concentrate their efforts to educate and inform pharmacists and physicians about the obvious advantages of this therapeutic system should complete this mission.

CONCLUSION

From the results obtained in the current study, we feel obliged to recommend some measures that may lead to a better outcome for the industry and the patient. To begin with, the critical situation of the Palestinian territories includes the constant presence of road blocks and check points, which represent major obstacles for the freedom of movement of individuals and transportation of goods, including medical supplies. This fact entails that Palestinian drug manufacturers should consider to reduce the size of their products and to avoid the use of fragile and bulky packaging containers, which, in general, will result in lower bulk and weight of the transported goods. With this measure being taken, a reduction of transportation costs, both on the local and international levels, may be achieved as well as making the process a relatively smoother one. Secondly, the transformation of many liquid preparations for a number of drugs into TTS formulations has many advantages, such as better portability, safety and ease of application. The ease of application of TTSs is especially important for patients traveling from one place to another while carrying their medications as well as saving space, both in industry stores and pharmacy shelves. Moreover, the use of TTSs is expected to result in a reduction of compliance problems in many patients of different age groups. It is advisable that more attention be given to TTSs as a safe and effective therapeutic system for a wide variety of pharmaceutically active ingredients. Pharmaceutical companies are encouraged to re-evaluate this issue and

to pay more public attention to it through condensed and scientific efforts of their medical representatives in order to change and improve the knowledge of many of the pharmacists and physicians who do not possess the proper information. This matter being accomplished will definitely have a positive effect on the sales of their marketed products.

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