



## PRACTICE REPORT

# Attitude and perception of patients and health care practitioners toward oral sustained release dosage forms in Palestine

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### KEYWORDS

Sustained release dosage forms;  
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**Abstract** *Aim:* To evaluate the knowledge of health professionals in Palestine regarding the advantages of sustained release dosage forms (SRDFs) over conventional therapy.

*Methods:* Data were gathered from a questionnaire that was handed out to community pharmacists, physicians and patients. Pharmaceutical industry decision makers were enrolled in this study. Data were analyzed using the SPSS.

*Results:* Pharmacists (92.9%) and 89.2% of physicians thought that SRDFs improve patient compliance. 81.5% of pharmacists and 77% of physicians were in agreement regarding the capacity of SRDFs to maintain therapeutic activity during night. In this study, 81.5% of pharmacists and 81% of physicians believed that SRDFs provide further advantage with psychiatric patients who forget to take their medications. Pharmacists (63.1%) and only 63.5% of physicians believed that SRDFs yield a time saving for nurses who use SRDFs in hospital. Only 45.3% of physicians and 43.4% of pharmacists thought that SRDFs result in cost saving due to better disease management. Pharmacists (95.2%) and 95.9% of physicians agreed that SRDFs could be the right choice for faith patient's who must take their medication during the month of Ramadan. Pharmacists (66.7%) and 50.7% of physicians recognize that SRDFs may be unsafe if they are improperly formulated. Bad swallowing was also recognized as inconveniences of SRDFs by 67.9% of pharmacists and 57.3% of physicians. Given the above advantages, 75% of patients showed economical problems regarding the cost of the single course therapy of SRDFs and 100% of interviewed patients were enthusiastic about the advantage of SRDFs during Ramadan.

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*Conclusion:* The advantages of SRDFs are not completely understood by Palestinian health professionals. Pharmaceutical industries should pay more attention to the development and advertising of SRDFs due to the valuable advantages of these dosage forms.

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## 1. Introduction

Drugs are often administered on scheduled bases to maintain the therapeutic level of pharmaceutical active ingredient in plasma or tissue in order to obtain a constant therapeutic effect over an extended period of time. This can be achieved with different dose and dosing interval. From the point of view of patient compliance, however the dosage regimen of orally administered drug may be considered to be optimal when the therapeutic effect is maintained for the desired duration of treatment at the lowest frequency of administration (de Haan and Lerk, 1983; Allen et al., 2005). This last desire can be achieved by using oral sustained release dosage forms (SRDFs) such as tablets and capsules. In fact, these dosage forms are commonly administered only once or twice daily, compared to the counterpart immediate release dosage forms (IRDFs) that have to be taken three or four times daily to achieve the same therapeutic effect. Typically, SRDFs provide immediate release of a portion of the drug that promptly produces the desired therapeutic effect, followed by gradual release of additional amounts of drug to maintain its therapeutic effect over a predetermined period. Consequently this optimizes the biopharmaceutic, pharmacokinetic and pharmacodynamic properties of the drug in such a way that its utility is maximized through reduction in side effects and control of condition in the shortest possible time (Stepenskya et al., 2001). These fascinating dosage forms have gained further importance and so they have been increasingly used in the last decades. In fact, SRDFs medications offer many clinical and convenience advantages for patients as compared to immediate-release IRDFs. Among these:

- (i) Improving patient compliance, since usually only one tablet has to be taken daily (Genton, 2005; Hale et al., 2007; Van Assche et al., 1990).
- (ii) Maintaining therapeutic activity during night (Aulton, 2007).
- (iii) Time saving for nurses who use SRDFs in hospital (Aulton, 2007).
- (iv) Providing further advantage with psychiatric patients who forget to take their medications (Keith, 2006).
- (v) Cost saving due to better disease management (Ward et al., 2007; Sinha et al., 2009; Das and Das, 2003).
- (vi) SRDFs are the right choice for faithful patients or Muslims who must take their medication during the month of Ramadan (a month of fasting, is a daily abstinence from any food, beverage, or oral drug from dawn to sunset).

Unfortunately, only drugs that have the appropriate physico-chemical characteristics (based on suitable biological half-lives or/and drugs that requires specific requirements for their oral absorption) are candidates for sustained release formula-

tions (Ramteke et al., 2006). Factors such as unsafety, due to over dosage, if SRDF is improperly formulated and improper swallowing, due to the large size of SRDFs, were the main problems of these dosage forms (Cornish, 2005; Andersen et al., 1995; Overgaard et al., 2001; Wamberg, 1988; Hey et al., 1983).

Despite these problems the improvement in patient compliance for long-term therapy encouraged many pharmaceutical companies to develop SRDFs for many pharmaceutically active ingredients. In fact, in the past recent years, there have been several financially successful passive SRDFs including those of carbamazipina, clarithromycin, verapamil, ciprofloxacin, clonidine and tramadol. This commercial success has generated further interest to expand the scope of therapeutics for the oral sustained release. In the light of what was mentioned above regarding these dosage forms, we decided to evaluate the attitudes of Palestinian health professionals and their assessment toward the advantages and disadvantages of SRDFs in the pharmaceutical field.

## 2. Materials and methods

This study was based on a questionnaire that was composed of three sections. The first part was a table where health professionals were asked to fill in details with trade names of oral SRDFs present in the Palestinian market, their manufacturing companies and the active ingredients contained therein. The second part was composed of another questionnaire which was filled by patients who were asked to comment about the following two statements: (i) the cost of SRDFs and (ii) the administration of medication during Ramadan. The third part was also a table where the health professionals were asked to comment on a statement regarding the advantages of SRDFs such as improving patient compliance, giving controlled release, maintaining therapeutic activity during night, time saving of hospital nurses, providing further advantages with psychiatric patients who forget to take their medications. Cost saving due to better disease management and being the best alternative to conventional IRDFs during Ramadan for faith Muslims or other faiths including Judaism and Hinduism were considered additional advantages of these dosage forms. Health professionals were also asked about the disadvantages of SRDFs, such as irritation and sensitization, and the limitation of this therapeutic system to only those drugs with appropriate physico-chemical properties. The questionnaire was handed out during the period of November 10th through December 10th, 2009. 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 (SPSS 16), (SPSS Inc., Chicago, IL, USA).

### 3. Results

#### 3.1. Physicians' and pharmacists' attitudes

The questionnaire was distributed throughout the cities of the west bank where it was filled by 148 physicians and 168 community pharmacists. Pharmacists were also asked to write the name of SRDFs available in their pharmacy. In addition, 16 decision makers also responded by filling the specified part of the questionnaire. Only fourteen (14) different trade names were found in the Palestinian market, three of which were carbamazepine-sustained release, while the remaining SRDFs were represented by one active ingredient for each trade name. Only three of these SRDFs were produced in Palestine, one of which (Tramal Long) was produced by Pharmicare under the license of Grunenthal GmbH (Table 1).

Among the participant, 92.9% of pharmacists and 89.2% of the physicians reported that SRDFs improve patient compliance. The results obtained also showed that the majority of community pharmacists (81.5%) and most physicians (77%) were in agreement regarding the capacity of SRDFs to maintain therapeutic activity of the drug during night (Table 2). In this study, equal percentages of the physicians and pharmacists (81.5% and 81%) agreed that SRDFs may provide further advantage with psychiatric patients who usually forget to take their medications. This also results in improvement of patient compliance better than the corresponding counterpart IRDFs that may have to be administered three or four times daily to achieve the same therapeutic response (Table 2). Most of the community pharmacists (63.1%) and physicians (63.5%) believed that the use of SRDFs results in time saving for nurses (Table 2). Almost

a minority of pharmacists and physicians (43.4% and 45.3%), respectively had the same opinions regarding the cost saving due to better management of the disease when SRDFs are used instead of other oral IRDFs containing the same pharmaceutically active ingredients. With respect to the statement of "SRDFs could be the right choice for faith patients who must take their medication during the month of Ramadan without stopping their fasting". About the absolute majority of physicians and community pharmacists who participated recognized that SRDFs are the right choice for these faith patients (Table 2). On the other hand, most pharmacists (66.7%) and about one half of physicians (50.7%) recognized that the main limitation of SRDFs is their unsafety if they are improperly formulated (Table 2). Regarding the large size of some SRDFs which may result in difficulty swallowing, 67.9% of pharmacists and 57.3% of physician agreed.

#### 3.2. Patients viewpoint

This part of study was composed of only two statements. The first one discussed the higher cost of the single course therapy of SRDFs in comparison with IRDFs containing the same active ingredients and how this cost can be overcome by better disease management and less side effects. Here, the majority of patients (75%) understood and were agreed with this discussion. The second statement discussed the advantage of SRDFs during Ramadan, since they can take these medications orally and so patients can adhere to fasting. Here one hundred percent of interviewed patients were enthusiastic to hear about such pharmaceutical innovation.

#### 3.3. Industrial personnel viewpoints

Table 3 shows industrial personnel questionnaire in which they were asked to pick the reasons pharmaceutical companies have developed very small number of SRDFs. One half of interviewed pharmaceutical decision makers thought that the reason behind the scarce or non-development of these dosage forms was lack of technology or specialized personnel to develop SRDFs. A high percentage of the questioned personnel (71.4%) believed that poor development of SRDFs may be due to either strategic company decisions or to the high cost of production. Only 7.14% of the interviewed decision makers believed that bad understanding of health professionals regarding the importance of SRDFs in the therapeutic field relies on the strategy of non-developing SRDFs.

### 4. Discussion

The number of SRDFs 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 SRDFs but they still need to improve their knowledge on some other points mentioned in this study. But the result of this study should encourage the increase in the number of these formulations in the Palestinian pharmaceutical market and thus improve the efficacy of the therapeutic drug treatment considering the previously mentioned advantages which play a fundamental role in the improvement of drug compliance.

**Table 1** Sustained release dosage forms available in the Palestinian pharmaceutical market.

Trade name	Pharmaceutical active ingredient	Manufacturer
Klacid XL	Clarithromycin	Abbot
Efexor XR	Venlafaxine	Wyeth
Adizem CD	Diltiazem HCl	Rafa
Delatam	Diltiazem HCl	Abic
Anafranil	Clomipramine	Novartis
Lescol XL	Fluvastatin	Novartis
Etopan XL	Etodolac	Taro
Tramal	Tramadol HCl	Pharmacare, under license of Grunenthal
Decongex SR	Chlorpheniramine Maleate and pseudoephedrine HCl	Belpharm
Gripmin SR	Pseudoephedrine HCl	Jerusalem
Omnice	Tamsulosine	Astellas Pharma
Omnice-Ocas	Tamsulosine	Astellas Pharma
Trental	Pentoxifyllin	Aventis
Timonil	Carbamazepine	Megapharm
Teril	Carbamazepine	Taro
Tegretol CR	Carbamazepine	Novartis
Osmo-Adalat	Nifedipine	Perrigo (Agis)
Xatral SR	Alfuzosine	Sanofi Aventis
Depalept Chrono	Sodium valproate and valproic acid	CTS
Ikapress SR	Verapamil	Teva
Pentasa	Mesalamine	Fairing

**Table 2** Comments of physicians and pharmacists regarding the advantages and disadvantages of SRDFs.

Statements asked to physicians and pharmacists regarding the characteristics of TTS	Pharmacists			Physicians		
	Agree (%)	Disagree (%)	Uncertain (%)	Agree (%)	Disagree (%)	Uncertain (%)
SRDFs improve patient compliance, since only one tablet has to be taken daily	92.9	5.4	1.7	89.2	6.1	4.7
SRDFs maintain therapeutic activity during night	81.5	14.3	4.2	77	14.9	8.1
SRDFs provide advantages with psychiatric patients who usually forget or refuse to take their medications	81.5	13.7	4.8	81	12.2	6.8
Time saving for nurses hospital due to the use of SRDFs	63.1	18.5	18.5	63.5	20.9	15.5
Cost saving due to better disease management when SRDFs are used	43.4	31.0	25.6	45.3	37.8	16.9
SRDFs could be the right choice for faith patient's who take their medication during the month of Ramadan	95.2	1.8	2.4	95.9	1.4	2.7
Unsafety due to over dosage if SRDF is improperly formulated	66.7	17.3	16.1	50.7	44.6	4.7
Bad swallowing due to the large size of SRDFs	67.9	22	10.1	57.3	32.5	10.2

**Table 3** The comments of industrial personnel regarding the reasons of the poor development of SRDFs.

Statements asked to industrial personnel regarding the reason of not developing chewable tablets	Agree (%)	Disagree (%)	Uncertain (%)
Very costly	71.4	21.4	7.2
SRDFs are not fully evaluated and accepted by physicians and pharmacists	7.1	42.9	50
Lack of technology or specialized personnel	50.0	42.9	7.1
The company has more important strategies	71.4	28.6	0.0

In fact, the increase in patient's compliance due to the use of SRDFs compared with immediate release formulations, containing the same pharmaceutically active ingredient, is a very important factor in the selection of the treatment. In fact, SRDFs play an important role in this contest, since these dosage forms maintain their therapeutic activity during night and this will avoid the awakening of patients during night to take their medication. At the same time, a further advantage is achieved when SRDFs are used in the field of psychiatric patients who usually forget or refuse to take their medication as reported by the majority of interviewed physicians and pharmacists. With this advantage, it is expected that a preferential attitude toward these dosage forms is practiced when supplying certain medications in psychiatric clinics.

Another very important result to be discussed is the cost saving due to time saving of nurses who use SRDFs in hospitals where most of pharmacists (63.1%) and physicians (63.5%) agreed with this issue. These results should be discussed carefully since, knowing that time saving to nurses in the hospitals should be achieved when SRDFs are used. This may result in a decrease in the number of employed nurses which return in cost saving for hospitals who use these dosage forms. This point should not be isolated in terms of cost from the obtained results regarding the cost saving due to better

management of therapy when SRDFs are used. Here unfortunately, a small number of both pharmacists and physicians agreed with this point. Probably these results can be interpreted when pharmacists and physician consider the cost of the single course therapy, which is usually higher than the corresponding IRDFs. As the better disease management was improved due to avoidance of drug plasma fluctuation and minor probabilities of forgetting the dose administration, these factors associated with the discussed higher patient compliance should result in better disease management and so cost saving for patient and society alike. Concerning the use of SRDFs during Ramadan, about the absolute majority of interviewed pharmacists and physicians consider SRDFs as an ideal choice for those patients who refuse to stop fasting (in Ramadan) if they have to take their medication during day. This clearly results in worsening of their medical conditions. But once again the use of the corresponding SRDFs should be an ideal alternative since patients are able to take their dose after the sunset. This important result will clearly return in high economic outcome for pharmaceutical industries that produce SRDFs considering that Islam is the world's second largest religion and has 1.57 billion adherents, making up 23% of the world population (Miller, 2009). According to these findings, we recommend pharmacists and physicians to pay more attention to SRDFs and to talk with patients about these advantages in order to convince them to shift their therapy from IRDFs toward SRDFs. In fact, this will be important for pharmacists and physicians since the high patient compliance achieved from SRDFs will improve the trust between patients and caregivers which means again higher medical benefits. Again the results obtained from the interviewed patients should encourage doctors and pharmacists to push in such direction, since the majority of patients do not have problem with the higher cost of the single course therapy. In fact these patients accepted the idea of overcoming and cost saving due to better disease management and less side effects when they use SRDFs instead of IRDFs. Further encouragement was obtained from the enthusiasm that was showed by the interviewed patients regarding SRDFs and Ramadan. In fact, these patients expressed their satisfaction to hear about such formulation and they said that in future they will ask

doctors and pharmacists about this alternative dosage forms especially during Ramadan. Regarding the results related to the unsafety of SRDFs if these are improperly formulated, most pharmacists and physicians agreed with this. In fact, SRDFs may produce accidental toxicity which is difficult to be treated if these formulations accidentally release their total content of pharmaceutically active ingredient. Regarding the results related to the large size of some SRDFs and the effect of this issue on the improper swallowing, most pharmacists and physicians agreed with this point. In fact, administration of oral dosage forms to children presents a challenge for both health professionals and patients equally. Also for many adults, it is not always easy to swallow 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 (Cornish, 2005; Andersen et al., 1995; Overgaard et al., 2001; Wamberg, 1988). Thus, this issue should be considered seriously by manufacturers in order to decrease the large size of SRDFs. Regarding the results of the questionnaire given to decision makers in the pharmaceutical industry, it was interesting to see that this category has recognized precisely two reasons for the non-development of SRDFs. In fact, 71.4% of them reported that the high cost of production is the obstacle. Another obstacle was the strategies of the industries that do not consider SRDFs development as an important enterprise. Another obstacle is represented by the lack of technology or specialized personnel to develop such dosage form but here only one half of interviewed decision makers recognized this point. However, the first two reasons can be solved by encouraging them to do investment in the production of SRDFs especially when we consider the high patient compliance and the use of these dosage forms during Ramadan month as was discussed earlier in this study. Regarding the lack of technology and specialized personnel, the 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. Concerning the second reason, SRDFs are not fully evaluated and accepted by physicians and pharmacists, this point should not be absolutely a serious problem, since the absolute majority of the interviewed pharmaceutical decision makers do not agree with this point. In fact, also the first part of this study shows that the interviewed pharmacists and physicians have a positive idea about the many advantages of SRDFs. 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 such dosage forms should resolve this issue. Moreover, pharmaceutical companies should ask and train their medical representative to educate patients toward the benefits that should be achieved from using SRDFs, especially regarding the cost of therapy which as discussed previously may discourage the patient if he thinks only to the economical part of the course therapy without considering the great medical benefits that he should achieve. This is true again when we consider the antibacterial and antiviral agents. Also, these medical representatives should point the light on the great advantage and happiness that faith Muslims patients find when they know that there is no need any more to stop their fasting during Ramadan if they use SRDFs instead of IRDFs. In fact, this was seen in the part of study related to patients viewpoints.

## 5. Conclusions

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. Firstly, the transformation of many IRDFs for a number of drugs into SRDFs has many advantages, such as better compliance and less frequent administration. The decrease in frequency of administration of SRDFs 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 SRDFs during Ramadan may result in better disease management and in higher economical outcome for pharmaceutical industries that produces SRDFs. Therefore, it is advisable that more attention be given to SRDFs as an excellent choice 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. Also they should aware population regarding these advantages so patient can ask medical advice from his physician or pharmacists regarding this issue. This matter being accomplished will definitely have a positive effect on the sales of their marketed products.

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