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Attitudes, Knowledge and Practices of Health-Care Practitioners Toward Splitting or Crushing Oral Solid Dosage Forms in Palestine: Safety and Therapeutic Implications

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Dedication

To my beloved mother, father, wife, sisters, and all who gave me help and support throughout my life.

الاقرار

انا الموقع ادناه موقع الرسالة التي تحمل العنوان:

Attitudes, Knowledge and Practices of Health-Care Practitioners Toward Splitting or Crushing Oral Solid Dosage Forms in Palestine: Safety and Therapeutic Implications

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Declaration

The work provide in this thesis, unless otherwise referenced, is the researchers own work, and has not been submitted elsewhere for any other degree or qualification.

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List of Abbreviations

BAPEN	The British Association for Parenteral and Enteral Nutrition
CR	Controlled Release
ER	Extended Release
GIT	Gastro Intestinal Tract
ISMP	The Institute For Safe Medication Practices
LA	Long Acting
MR	Modified Release
MOH	Ministry of Health
NGOs	Non Governmental Organization
OSDFs	Oral Solid Dosage Forms
OTC	Over The Counter
SA	Sustained Action
SR	Sustained Release
SRDFs	Sustained Release Dosage Forms
TR	Targeted Release
TD	Time Delay
TM	Time Release
UNRWA	United Nations Relief and Works Agency
XL	Extended Release

Attitudes, Knowledge and Practices of Health-Care Practitioners Toward Splitting or Crushing Oral Solid Dosage Forms in Palestine: Safety and Therapeutic Implications

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Abstract

Background: Tablet splitting and crushing is a widespread practice among health-care providers and patients for different reasons, such as: (i) increasing dose flexibility, (ii) making tablet parts easier to swallow, and (iii) allowing cost savings for medications. However, this practice may be dangerous because some formulations and classes of drugs are unsuitable for crushing or splitting and may cause significant problems, especially in drugs with low therapeutic indices.

Objectives: This thesis was conducted to examine the attitudes, knowledge and practice of pharmacists and nurses toward splitting or crushing oral solid dosage forms (OSDFs) in Palestine. It also aimed to determine the factors that affect health-care practitioners with regard to splitting or crushing OSDFs, in addition to determining the differences in attitudes and knowledge between nurses and pharmacists regarding this very important issue, and to determine the safety and therapeutic problems that resulted from splitting or crushing OSDFs.

Methodology: This is a self-administered cross-sectional questionnaire survey involving 550 respondents and was conducted during the period

May 2013 to August 2013 among pharmacists and nurses who work at community pharmacists and hospitals in the West Bank area of Palestine. Data were collected using a pretested questionnaire consisting of four sections and analysed using descriptive statistics and correlation.

Results: A total of 615 questionnaires were distributed and 550 were completed. About 67.3% of the pharmacists and only 5.6% of the nurses had good knowledge. Nearly 69% of the pharmacists and 36.4% of the nurses had a good attitude. There was a positive correlation ($p=0.002$, $r=0.18$) between knowledge and attitude scores among pharmacists. There was a positive correlation ($p<0.001$, $r = 0.24$) between knowledge and attitude scores among nurses. Approximately 83.7% of the pharmacists and 41.6% of the nurses had good practices.

Conclusion: This study has identified knowledge, attitude and practice gaps among health-care practitioners, especially among nurses. Therefore improving appropriate knowledge regarding splitting and crushing OSDFs is required by planning and developing programs for local health education purposes

Chapter one

Introduction

1. Introduction

1.1 Background

1.1.1 Advantages of splitting or crushing oral solid dosage forms

One of the significant current discussions from a medical and legal point of view is splitting or crushing oral solid dosage forms (OSDFs). Splitting OSDFs refers to the practice of dividing a tablet to provide a lower dose of the active ingredient or to obtain multiple smaller doses for many purposes. While crushing tablet refers to the process of converting tablets into powder by using suitable pharmacy tools such as mortar and pestle. These may provide several advantages. Patients usually split tablets for various reasons, such as: (i) providing the patient with the desired dose when the product is not available at the required strength, e.g. hydrochlorothiazide: the available dose is 25mg and the drug is commonly used in doses of 12.5mg, thus the patient needs to split the tablet to receive the smaller dose. Another example is converting atenolol tablets into capsules with the desired filling weight [1]. This practice is useful for children or older persons; (ii) slowing the titration of the medication to start therapy with the lowest possible doses and then starting to increase the dose until reaching the desired dose to enable toleration of the drug and reduce the incidence of side effects of certain drugs, e.g. with beta-blockers such as metoprolol used post myocardial infarction, patients cannot tolerate full doses of 50mg and instead are given 12.5mg, then the dose will be increased. The lowest dose available is 50mg, which necessitates the tablet being split into quarters to give the wanted dose [2]. Another example of the benefit of

splitting a tablet in slow titration is patients who are taking anticoagulation therapy with warfarin: patients require frequent dose changes to stay at an appropriate level of anticoagulation. Instead of purchasing more than one strength, patients resort to purchasing one strength and splitting the tablets to adjust the dose as required [2]; (iii) reducing medication costs; (iv) making the swallowing of large tablets easier [3-5]; (v) providing medication dose flexibility [6, 7]; (vi) crushing tablets is an acceptable method of medication administration for patients with swallowing problems due to the large size of the capsules or due to a bad taste or the number of tablets to be administered, and crushing tablets and mixing them with food is considered a convenient method of administration to individuals with memory loss or confusion [8].

1.1.2 Consequences of splitting or crushing OSDFs

It is important to realize the possible effects of tampering with drugs. Altering the design of dosage forms may cause a change in the pharmacokinetic and pharmacological effect of drugs [9]. There are some problems associated with splitting or crushing OSDFs. It creates hazards for health workers: splitting or crushing teratogenic drugs or carcinogenic drugs such as valganciclovir or methotrexate expose health workers to risks via the aerosolization of powder, in a similar way to some hormones, corticosteroids, mycophenolate and many other drugs [9]. In fact, powder dust is one of the major factors that must be controlled during the manufacturing of OSDFs, since this factor is responsible of cross

contamination and may cause serious hazards to operators. Splitting or crushing OSDFs may have a negative effect on drug stability; an example of that is nifedipine-coated tablets, as this drug is very light-sensitive when it has been crushed [9]. Proton-pump inhibitors such as omperazole and pantoprazole are enteric coated. This coat protects them from acidic environment of the stomach. This permit them to reach unchanged the site of absorption. The effect of the drug coating will be removed by crushing it and this will lead to decreasing the effect of the drug in the small intestine [10]. Changes in bioavailability are another problem associated with crushing OSDFs [9]. These changes may be very significant for drugs with a narrow therapeutic window such as carbamazepine or digoxin [9]. In fact one of the major disadvantages of sustained release tablets is due to the rupture of this design (coat or matrix) which cause the release of the content in the gastrointestinal tract (GIT) causing toxic levels of the active pharmaceutical ingredients.

For drugs that have a problem with their taste such as ciprofloxacin, clarithromycin, ibuprofen and sertraline, coating is utilized to hide their unpleasant bitter or anaesthetic taste [9]. Sugar coating, which contains a hard thick layer, may be used for coating drugs such as ibuprofen [9]. Film coating, which contains a thinner layer than sugar, is also used for coating many drugs such as ciprofloxacin, pseudoephedrine and cefuroxime axetil [9]. So crushing drugs that have a bitter taste may lead patients to reject taking drugs unless they are mixed with suitable food or drink [9]. In fact, clarithromycin is one of the worst bitter tasting drugs, this drug reaches the

salivary gland after being absorbed and distributed. This will result in a strong bitter aftertaste that may decrease patient compliance.

1.1.3 Formulation of drugs that should not be crushed

There is a strong correlation between splitting or crushing drugs and their dosage form, and some dosage forms, such as controlled release OSDFs, enteric-coated, extended release dosage forms and many other preparations must not be crushed or split [11].

1.1.4. Modified-release oral dosage forms (MR)

Conventional immediate release OSDFs, including tablets and capsules, are designed to release the medicament immediately after oral administration. In fact, there is no need for any especial formulate effort in order to modify the drug release pattern. These products generally show relatively rapid onset of action. Vice versa, the pattern of drug release from modified-release OSDFs is intentionally changed from that of conventional OSDFs in order to achieve the desired therapeutic response or to increase patient compliance. Accordingly, The term modified-release OSDFs was suggested to describe oral solid formulations such as tablets and capsules were the timing and/or the rate of release of the medicament were intentionally changed or programmed. In fact, MR dosage form is a formulation in which the medicament-release profile and/or location are chosen in order to improve the therapeutic efficacy and safety of the

medicament, objectives, which are not achieved by using conventional OSDFs [12].

1.1.4.1. Definition and abbreviations

Several terminologies and abbreviations are used under the umbrella of MR; many of them can be interchangeable. Some of these definitions and abbreviations are reported below [12].

- **Controlled-release (CR):**

These formulations are designed to release medicament at a constant rate in order to achieve plasma concentrations that remains nearly constant within time.

- **Extended release (ER):**

These dosage forms are designed to release the active ingredient slowly, and so plasma concentrations remain within the desired therapeutic level for an extended period of time.

- **Sustained release (SR):**

SR solid dosage forms contain a first initial dose which must be released immediately in order to achieve immediate onset of action. This initial release of the medicament is sufficient to provide a therapeutic dose soon after oral administration.

Then a second gradual release over an extended period of time which must cover all remaining period resulting in decrease of the number of drug administration.

- **Targeted-release (TR):**

This kind of dosage form consists of releasing the medicament at or close to the intended site of action. TR dosage forms may have either immediate or extended-release profiles.

- **Delayed release (DR):**

These formulations indicate that the drug is released at a later time after oral administration. This may be the case of enteric coated (EC) tablets were the drug should not be released in the stomach but in the intestine [9, 13].

1.1.4.2. Formulation of some MR dosage forms

1.1.4.2.1. Formulation of SR dosage forms

Oral SR formulations can be obtained via several mechanisms including: monolithic or matrix system, reservoir or membrane-controlled systems, osmotic pump systems. These are considered the most popular methods of achieving SR but other methods are now available [13]. The basic principle that governs all these methods is that after oral administration an initial dose is immediately released, and then the dissolved drug in the matrix or that surrounded by an appropriate membrane will diffuse from the tablet

(region of high concentration) to the lumen of the GIT (region of low concentration). This gradient of concentration is the driving force of the designed system [3, 9, 13].

1.1.4.2.1.1. Advantages and disadvantages of SR and CR dosage forms

SR dosage forms have many clinical and convenience advantages compared to immediate-release (IR) formulations. Among these are reductions of fluctuations in drug concentration and adverse side effects, especially those connected with rapid increase in peak serum concentration and local irritation; this results in improved drug tolerance, and maintains the drug concentration within the therapeutic level [14], reduces dose frequency, which means it is less likely to be misused or abused and increases compliance, reduces health-care costs and provides a more convenient dosing regimen [14]. Unfortunately, there are some problems related to the improper formulation of CR tablets such as the large size of the obtained tablets [11, 15-19] and the risk of dose dumping [13]. CR medication is also more expensive than IR formulation [13]. It is typically unsuitable for breaking, crushing or masticating, as doing so may result in the release of a dangerously large amount of the drug into the bloodstream [20, 21].

1.1.4.2.2. Formulation of Enteric-coated (EC) dosage forms

Enteric-coated tablets are prepared by coating the tablet with pH sensitive polymers. These polymers are insoluble at pH less than 5 and accordingly they remain unchanged in the stomach but they readily start to dissolve in more alkaline media in the small intestine [9]. This technique is applied to acidic sensitive drugs such as pancreatin and omeprazole in order to protect them from the acidity of the stomach [9]. It is also applied to drugs that may irritate the stomach such as non steroidal anti-inflammatory drugs [9]. It is also applied to other drugs such as sulfasalazine to postpone the onset of action to a specific site in the colon [9]. When enteric-coated tablets are crushed, the drug is released too early, which causes irritation to the stomach or the drug is destroyed by the stomach [9]. These considerations can be taken for SR oral dosage forms, since their splitting or crushing can result in complete release of the active pharmaceutical ingredients which results in drugs toxicity especially those with low therapeutic index.

Splitting or crushing extended-release or enteric-coated tablets is not recommended except for a few preparations, but this should only be done under the instruction of the drug manufacturer [9, 10, 22].

1.1.5. Sublingual, buccal and lozenge preparations

Sublingual and buccal dosage forms are preparations that perform their actions through a mucosal membrane; this causes a rapid increase in the concentration of the drug and also avoids the first-pass effect [9, 10]. If

these preparations are crushed, the bioavailability will be changed [9, 10]. Lozenges are a dosage form and are designed to stay in the mouth for 15 minutes in order to provide their effect in the mouth. If lozenges are crushed, their effect in the mouth will be decreased [9, 10].

1.1.6. Active Pharmaceutical Ingredients (APIs) that should not be crushed

Other classes of drugs that should not be crushed or opened must be considered, such as drugs with teratogenic, carcinogenic or cytotoxic properties, steroids, hormones, drugs causing an allergic reaction, staining of teeth and oral mucosa, nitrates, and drugs that act as irritants to the gastrointestinal tract, and also the properties of drugs must be considered, such as light or water sensitivity, and whether they have a very bad taste.

1.1.7. Safety and therapeutic implications of splitting or crushing OSDFs

Questions have been raised about the safety of splitting or crushing oral solid dosage forms that are designed as controlled-release and enteric-coated tablets [23]. A case has been documented in which a fatality occurred from the administration of crushed labetalol and extended-release nifedipine [24]. This case reported that a 38-year-old woman with many chronic diseases presented at hospital and was diagnosed with acute pulmonary edema and pneumonia [24]. She was given hydralazine, labetalol and nifedipineXL to control hypertension [24]. These drugs were

crushed and administered through a nasogastric tube [24]. The result was bradycardia and hypotension and the patient died after the administration of an additional dose of the same drugs the following morning. [24]. This means that the administration of crushed nifedipineXL causes severe hypotension and the co-administration of labetalol prevents a compensatory heart rate increase [24]. The extended-release mechanism was destroyed when the tablet was crushed, which causes a rapid increase in the concentration of drugs in the circulation [24].

In another case reported for a 78-year-old male patient who was given crushed sustained-release isosorbide mononitrate through a percutaneous endogastric tube, the patient complained of repetitive chest pain [25], but the symptoms disappeared when it was replaced by short-acting nitroglycerine three times a day [25].

In some capsules, where the extended-release properties are constructed into singular pellets contained in the capsules, it could be possible to open a capsule and use the content without crushing it [22]. Methylphenidate extended-release multiparticulate is an example of these constructed pellets [22].

1.1.8. Administration of drugs for patients with swallowing difficulties

Tablet splitting and crushing is one of many ways used by nurses and health practitioners to offer medications in the wanted dose. Recently researchers have been showing increased interest in this field, especially

the administration of crushed drugs for patients with swallowing difficulties [26]. Patients who are unable to swallow because of debilitating problems need a feeding tube for nutrition or the administration of drugs. There is little information about this issue, and it is associated with a risk of toxicity, occlusion and decreased efficacy [26]. Accordingly, the health practitioner must find the best way in order to administer drugs to patients through a feeding tube.

In 2003, the British Association for Parenteral and Enteral Nutrition (BAPEN) published guidelines on how to administer drugs via a feeding tube, which include: (i) try to use an alternative route instead of an oral route such as injection or discontinue the administration of the drug temporarily or switch to another drug that has the same effect and is available through another oral dosage form [26]; (ii) when no alternative route or drug is available, use liquid or dispersible tablets, and when the formulation has to be changed, the dose equivalencies must be taken into consideration; (iii) if tablets or capsules must be used, the properties of the formulation must be taken into consideration [26]; (iv) to avoid drug/food interaction, the medicine must be administered between eating; and (v) flushing techniques must be correct to avoid tube closure.

Issues related to swallowing difficulties would be mentioned; if there is no alternative route for administration, the solid dosage form is considered. Sometimes unlicensed drug use occurs. Crushed tablets may cause closure of the feeding tube, which may result in death or trauma to the patient.

When OSDFs are crushed it must be taken in to consideration that some formulations should not be crushed or opened such as unscored tablets, film- and sugar-coated tablets, enteric- or protective-coated tablets, sustained-release preparations, sustained-release granules, microencapsulated drugs, buccal or sublingual preparations and bitter-tasting tablets.

Another issue that must be studied is the drug/food interaction. The time of drug administration is very important in relation to the time of eating because the absorption of medicine is influenced by food in the feeding tube and the feeding tube itself. Avoiding drug/food interaction depends on whether the administration of food is continuous or intermittent and on the drug regimen. Phenytoin is an example of drugs where the absorption may be greatly decreased due to food/drug interaction or interaction with the feeding tube, especially as these drugs have a narrow therapeutic index, so this drug must be administered two hours apart from food.

1.2 Literature Review

1.2.1 Studies related to splitting or crushing OSDFs

To the best of our knowledge, a lot of discussion about splitting OSDFs can be found while the crushing practice has not been widely studied, but in recent years, there has been an increasing amount of literature on crushing OSDFs [26-28].

1.2.2 Germany and the Netherlands

Several studies have revealed the significance of inappropriate tablet splitting or crushing in primary health-care centers and hospitals. In a cross-sectional study by Quinzler et al. [29], which set out to determine the frequency and determinants of tablet splitting in primary health care in Germany, the study included 59 general practitioners and collected information on all the drugs of patients maintained on more than three drugs. The response rate was 82%, 24% of all drugs were split and 7.8% of all split tablets were unscored, 3.8% of the split tablets were not allowed to be split, and tablets of a higher price were twice as likely to be split. This study showed that splitting tablets in primary care centers is a frequent event due to economic considerations. In the same study nearly 1% of all tablets that were divided could not be fragmented or disintegrated.

Rodenhuis et al. [30] studied the rationale of scored tablets. The objective of this study was to determine the rationale of scored tablets and to determine the reason for splitting tablets. Two hundred and seventy-five prescriptions were collected and studied; also, patients who brought these prescriptions were questioned. The results show that 31% of the prescribed tablets were divided in most cases because the dose that needed to be divided was prescribed, while 30% of the tablets were divided under the patients' own initiative. The results also show that 13% of tablets were split for ease of swallowing, and 17% because the patient wanted to administer a lower dose. The results show that even unscored OSDFs were split for ease

of swallowing or because the dose prescribed were half the dose offered. Rodenhuis et al. [30] found that scored tablets still have an important role, and even when lower doses of tablets become available, there remain reasons for patients to subdivide tablets: for ease of swallowing, adapting the dose and economic considerations. Similarly, in 2006, Quinzler et al. published an article about tablet splitting. The paper mentions some benefits of tablet splitting, such as it provides dose flexibility, large-sized tablets can be easily swallowed when split and it reduces medication costs. Unfortunately not all tablets are suitable for splitting, e.g. unscored tablets, extended-release and enteric-coated tablets. Whether tablets are suitable for splitting depends on other things, such as the properties of the drug, the shape of the tablet, the shape of the score line, the patient properties, and the fact that most elderly patients are not able to split tablets properly. The authors advise looking at the shape of the tablet to detect whether the patient is able to split it or not, providing the patient with suitable information about how to split tablets properly and advising him/her on how to use a tablet splitter [29]. Another study was carried out at the university hospital of Heidelberg in Germany to assess the quality of information sources on the solid modification dosage form used in the wards of the hospital. The results show that 22 lists of information on drug modification were identified in the 79 wards. Each list contained errors, and on average 17.0% (range 8.0–32.3 %) of the brands listed had been withdrawn from the market or the information on crushing and/or suspending was inappropriate. The authors concluded that the lists posted

on the wards were often outdated and did not take into account the limitations/problems of preparing drugs on the ward and so there was inappropriate crushing information on ward lists: cytotoxic drugs, capsules and modified-release formulations were gravely neglected [31].

1.2.3 Palestine

Recently Zaid and Ghosh [32] evaluated the weight uniformity of commonly divided tablets produced by Palestinian pharmaceutical companies. They found that the practice of dividing OSDFs, which may provide economic and therapeutic benefits for the patients, may cause significant problems. They also concluded that the Palestinian pharmaceutical companies should comply with the new European Pharmacopoeia splitting regulations [32].

In another recent study, Zaid et al. [33] investigated whether there exists any difference between the European Pharmacopeia (Ph. Eur.) and the adopted United States Pharmacopeia (USP), and pointed out that harmonization between all pharmacopoeias regarding the weight uniformity test is recommended [33]. In another study the correlation between weight and content uniformity after splitting tablets of a low drug content product such as lorazepam was also investigated. [14].

1.2.4 Malta

The problem of OSDFs in patients with swallowing difficulties was studied by Bowman [26]. Bowman highlights some matters on how best to

administer drugs to patients with swallowing difficulties. He mentions some practical points on how to do this; these points include trying to use an alternative route, and using dispersible tablets or liquid preparations when no alternatives exist. If tablets have to be used, the stability of the formulation must be studied, bearing in mind that drug should be administered apart from feeding time, and that to avoid blockages of the tube, flushing methods must be correct. This article also studied issues related to solid dosage forms. Solid dosage forms are considered when no alternative route is available. Some classes of drugs should not be crushed or opened; these include drugs with carcinogenic, teratogenic or cytotoxic properties, steroids, pancreatic enzymes, hormone preparations and drugs causing allergic reactions. In addition to these classes, there are some formulations that should not be crushed; these include unscored tablets, enteric- or protective-coated tablets, sustained-release granules, chewable tablets, bitter-tasting tablets, film-coated tablets and sustained-release preparations. The properties of drugs must also be considered before tablets are crushed, such as water sensitivity or light sensitivity. Some medication may cause irritation to the mucosa oral or gastric region when crushed, so the site of entry must be taken into consideration. The same thing must also be considered when splitting tablets, as unscored tablets must not be split. The same thing is true for opening capsules as the powder may be light-sensitive, such as in the case of nifedipine or enteric-coated granules, which it is forbidden to crush. Bowman concluded that the administration of drugs

through a feeding tube requires an experienced nurse and each drug to be stable, and its effect must be considered before crushing OSDFs [26].

1.2.5 Australia

In 2013, Mercovich and colleagues studied dosage form modification in elderly care and whether it is safe to crush or not. The aim of this study was to explore solid dosage form modification in elderly care facilities, and examine the knowledge of health-care professionals and the references and resources available to them. The study was carried out by observation of medication rounds in a convenience sample and assessing staff knowledge of crushing tablets [27].

The most commonly modified modifications were vitamin D capsules, paracetamol IR tablets, levodopa+carbidopa tablets, warfarin tablets, metformin IR tablets, furosemide and spironolactone. In 160 observations across six medication rounds, 75 medications were modified by a nurse and 32% of these were identified as inappropriate. The observed medications that should not be crushed according to the Australian Don't Rush to Crush Handbook were levodopa+carbidopa, warfarin, dompridone, amiodarone, baclofen, desvenalfaxine, donepezil, esomeprazole, hydralazine, lansoprazole, letrozole, oxycodone SR, ramipril and sodium valproate. The reasons for preventing crushing were altered release characteristics, reduced drug stability, risk of harm from variation in the drug quantity administered, manufacturer's recommendation and altered drug absorption profile [27].The method used

for crushing and mixing leads to spillage and inaccurate dosing. The results show a lack of knowledge on how to use the resources. This study concluded that if we want to reduce the observed high prevalence of mistakes when tablets are crushed, we must improve staff training regarding using available resources [27].

1.2.6 USA

A case study was conducted by Schier et al. [24] about a fatality that occurred from the administration of labetalol and crushed extended-release nifedipine. This case reported that a 38-year-old woman with many chronic diseases presented to hospital and was diagnosed with acute pulmonary edema and pneumonia. The patient was given hydralazine, labetalol and nifedipineXL to control hypertension.These drugs were crushed and administered through a nasogastric tube. The result was bradycardia and hypotension and the patient died after the administration of an additional dose of the same drugs the following morning. This means that the administration of crushed nifedipineXL causes severe hypotension and the co-administration of labetalol prevents a compensatory heart rate increase. The extended release mechanism was destroyed when the tablets were crushed, which causes a rapid increase in the concentration of drugs [24].

In another case study conducted by Hider and Shehap in 2000 about the effectiveness of modified-release isosorbide mononitrate affected by incorrect use reported for a 78-year-old male patient who was given

crushed sustained-release isosorbide mononitratethrough a percutaneous endogastric tube, the patient complained of repetitive chest pain, but the symptoms disappeared when it was replaced by short-acting nitroglycerine three times a day [25].

Another recent study conducted by Gill and colleagues [8] about crushing or splitting medications focused on unrecognized hazards. The paper revealed that tablet splitting has many benefits if the tablet is suitable for splitting and the patient splits it correctly, but splitting unsuitable medications such as extended-release formulations is problematic. Crushing inappropriate medication that should not be crushed for ease for administration in liquid or with food is problematic and potentially harmful. Care providers who take care of old people need to clarify the dosing schedule and the route of administration and re-evaluate the medication treatment regimen.

In a review article conducted by Freeman et al. [34] about tablet splitting weight and content uniformity, the paper revealed that the practice of tablet splitting is increasing, which causes variation in drug distribution. Although this practice has the potential to save money, the appropriateness of tablet splitting must be evaluated. Almost all of the studies associated with tablet splitting show large fluctuations in weight/dose, but there are few studies on the variability of narrow therapeutic index drugs. So the clinical importance of these variations is not applicable nationally through medication classes.

In 2006, Noviasky and his team published a paper about which medications can be split without compromising efficacy and safety. The authors reported that split lisinopril tablets are as effective as whole tablets of the same dose for hypertension based on small randomized crossover studies, and similarly, split atrovastatin, lovastatin and simvastatin tablets, are no less effective for cholesterol reduction based on retrospective cohort studies [35]. The authors also reported that extended-release tablets, enteric-coated tablets and tablets that cannot be split accurately are not appropriate for splitting according to observational studies. They reported that the accuracy of splitting tablets depends on the device used and the skill of the user based on observational studies. They also reported that splitting scored tablets is efficacious and safe, but cost savings are often limited. The American Medical Society and American Pharmacists Association recommended against splitting tablets that are modified release, combination products, unscored, film coated, friable or dose-critical [35].

1.2.7 Canada

Bachynsky et al. [2] examined the practice of splitting tablets as a method for cost saving. Two hundred prescription products in Canada were evaluated for their potential for tablet splitting to reduce costs. The authors found that costs were saved for only 15 out of the 200 products. They concluded that tablet splitting appears to have limited benefits as a cost-saving strategy; small products appear to be suitable for splitting and also

have the potential for saving money. Another issue that must be taken into consideration is patient compliance and the risk of an incorrect dose [2].

In 2005, Cornish published an article about avoiding crushing, and the hazards of medication administration in patients with dysphagia or using a feeding tube. The author mentions two cases. In case one, a patient was admitted to hospital with acute dysphagic stroke; he was given a sustained-release preparation of oxycodone. The patient was unable to swallow the whole tablet, and because of a lack of knowledge of the characteristics of the drug, the tablet was crushed for ease of administration. Crushing the tablet destroyed the drug's sustained-release properties and led to sedation and respiratory depression [11].

In a second case, a patient was discovered to have reflux esophagitis and was given enteric-coated omeprazole through a feeding tube, and after one month of therapy the patient's symptoms had not resolved. Crushing tablets destroys the protective coating, which results in loss of efficacy. The author mentions that 70% of errors related to medication dosage forms in hospital were due to failure to specify the extended-release formulation when it was intended, e.g. administration of nifedipine 60mg once daily instead of nifedipine XL [11]. The author concluded that with increased recognition of this problem and increased knowledge for health-care providers, along with enhancements to medication use regulation, adverse events related to sustained-release and enteric-coated formulations of drugs can be avoided [11].

1.2.8 Taiwan

A recent study conducted by Chia-yu and colleagues studied the association between physician specialty and the risk of prescribing inappropriate pill splitting. They evaluated the prescriptions that involved extended-release or enteric-coated formulations in Taiwanese medical centre over five months in 2010 [36]. In this cohort study there were 1252 inappropriate prescriptions discovered at a percentage of 1%. Antidiabetic agents, anticardiovascular agents and central nervous system agents were the most common classes of drugs discovered as being inappropriately split. The study revealed that 87% of inappropriate prescriptions were prescribed by internists and the rate of inappropriate tablet splitting was the highest among endocrinologists, nephrologists and cardiologists. The authors concluded that inappropriate tablet splitting in medical prescriptions is common, and this practice may be due to a lack of knowledge of special formulations that cannot be split [36]. The authors suggested that health-care providers should make further efforts to employ safe ways to prevent or reduce the occurrence of inappropriate splitting of OSDFs [36].

1.2.9 Oral solid dosage forms that should not be crushed

The Institute for Safe Medication Practices (ISMP), a non-profit organization based in suburban Philadelphia in the USA educating the health-care community and consumers about safe medication practices, ISMP has published lists of oral solid dosage forms that should not be

crushed, and these were last updated in August 2013. The lists are not meant to represent all products either by generic or trade names. So these lists are considered to be indicative lists for nurses, pharmacists, doctors and other health professionals for reference [10].

1.2.10 Studies related to measuring knowledge, attitudes and practices

A recent study conducted by Akram and Mullen [28] discussed pediatric nurses' knowledge and practice of mixing medication into foodstuff. The aim of this study was to examine nurses' knowledge and practices regarding drug stability issues when mixing medication in to foodstuff. Thirteen nurses from pediatric mental health and general pediatric nurses were included in the study with a response rate of 71%. All of the nurses except one had mixed medication with food before administration [28]. The common foodstuffs used were squash, fruit juice and fruit yoghurts. The proportion of nurses that did not feel adequately knowledgeable about mixing drugs and stability issues was 27%. The interviews show a knowledge deficit in the nature of the problem clinically. The authors found that co-mixing of medication into foodstuff is a common practice. The majority of nurses were unaware of potential drug stability/degradation issues and/or the clinical impact of these practices. The study also discovered gaps in undergraduate nursing and medical education on the subject of medication administration [28].

A cross-sectional study conducted by Zaid [14] aimed at assessing the attitude and perception of patients and health-care practitioners toward oral

sustained-release dosage forms (SRDFs) in Palestine. This study found that 92% of pharmacists and 89% of doctors believe that SRDFs improve patient compliance; 77% of the physicians and 81.5% of the pharmacists agree that SRDFs can maintain therapeutic activity during the night; 81.5% of the pharmacists and 81% of the physicians think that SRDFs help psychiatric patients to take medication with less frequent doses; 95.2% of the pharmacists and 95.9% of the physicians agree that SRDFs could help patients who have to take medication during Ramadan. The author concluded that the usefulness of SRDFs is not completely understood by Palestinian health professionals. The problem rests mainly with the drug companies: they must give more attention to educating health-care professionals and also patients about the valuable benefits of this formulation [14].

Another study measured the attitudes towards tablet splitting of patients who currently split tablets [37]. The findings of this study confirmed that a large percentage of patients on combination therapy divide tablets. The findings indicated that a high frequency of inappropriate tablet splitting was indicated by physicians and not by the patients themselves [37]. Indeed, these findings also indicate that many patients were not aware of the importance of this issue [37].

1.3 Problem statement and rationale for the study

1- Previous research in the world has produced few studies about this issue and this study is considered to be the first in Palestine to measure the

knowledge, attitudes and practices of health-care practitioners regarding crushing and/or splitting OSDFs.

2- Assessing knowledge, attitudes and practices will help MOH, pharmaceutical and nurse associations to argue for mandatory training courses about when it may be appropriate to consider crushing or splitting OSDFs, and the best ways to do it.

3- This study will help people at the university to design multidisciplinary course in clinical toxicology and clinical pharmaceutics for ongoing nurse and pharmacy education that meets Palestinian nurse and pharmacy practice situations.

1.4 Research aims and objectives

1.4.1 The main objectives of the current study were:

1- To measure the attitudes of health-care practitioners toward crushing and/or splitting oral dosage forms in Palestine.

2- To measure the knowledge of health-care practitioners regarding crushing and/or splitting oral dosage forms in Palestine.

3- To measure the practices of health-care practitioners regarding crushing and/or splitting oral dosage forms in Palestine.

1.4.2 The sub-objectives of this study were to determine the factors that affect the attitudes of health-care practitioners toward splitting or crushing OSDFs, to determine the differences in attitudes and knowledge between

nurses and pharmacists regarding this very important issue, and to determine the safety and therapeutic problems that resulted from splitting or crushing OSDFs.

1.5 Significance and benefits of the study

This study is very important because it will increase the awareness of health-care practitioners toward splitting or crushing OSDFs, the appropriate decision and the best way to consider crushing or splitting tablets. The results of this study are a first attempt to characterize healthcare provider's knowledge, attitudes and practices toward splitting or crushing OSDFs, and to identify demographic characteristics associated with particular knowledge, attitudes and practices in Palestine, and this will give a body of data that will inform the approach to future management strategies and further research.

It will also highlight the problem of using drugs that are incompatible with the enteral route in patients using feeding tubes. It also increases the knowledge about the best methods that can be used to crush tablets without losing a high percentage of powder. In addition, it will evidence the safety of crushing OSDFs, especially with narrow therapeutic index drugs. Furthermore, this study will show whether there is a problem related to the effectiveness of the drug after dividing or crushing pills, especially if the patient suffers from a chronic disease and needs to use the drug for a long time.

Chapter Two
Material and Methods

2. Methodology

2.1 Study design and study area

This is a questionnaire-based cross-sectional analytical study; it is designed to measure the attitudes, knowledge and practices of pharmacists and nurses toward crushing or splitting OSDFs.

Palestine consists of two zones separated geographically: the West Bank and the Gaza Strip, with a total population of about three million inhabitants. Nearly 62% live in the West Bank and 39% live in the Gaza Strip. The West Bank is divided into three regions and 11 governorates. The north area comprises: Jenin, Tulkarm, Nablus, Qalqilya, Tubas and Salfit; the middle area comprises: Jerusalem, Ramallah and Jericho; the south area comprises: Bethlehem and Hebron [38].

This study was conducted in the West Bank of Palestine from May 2013 until August 2013. The authors acquired a list of the names of hospitals and their addresses from the Ministry of Health, and obtained a list of names of all community pharmacies and their addresses from the Palestinian Pharmaceutical Association. Based on the lists, the authors visited the following governorates in the West Bank: Nablus, Jenin, Tulkarm, Qalqilya, Tubas, Ramallah, Bethlehem and Hebron [38].

2.2 Population of the study

The population of the study was nurses who work in hospitals in the West Bank and pharmacists who work in community pharmacies and hospitals in the West Bank. Community pharmacists comprise one of the most important sectors of health-care professionals: in addition to their role in providing drugs, they are also considered a source of information about health and drugs. The West Bank, which is located west of the River Jordan, has a total population of three million and is divided in to three regions – north, south and middle – in 11 governorates. There are 3217 registered pharmacists in the West Bank and the majority of them work in the private sector. Others work in hospitals, clinics, and pharmaceutical industries and companies.

There are 6340 registered nurses in the West Bank of whom 60% are women. The percentage of nurses who work in the government is 40%. There are seven universities in the West Bank from where nurses with different specialties' graduate [38].

The absence of ongoing pharmacy education creates negativity regarding their role in educating the public. Many studies show that the public trusts information provided by pharmacists. A study carried out in the West Bank found that the public has a good perception of community pharmacists [39]. Another study conducted in the West Bank showed that 30% of pregnant women take over-the-counter (OTC) drugs from community pharmacies and 45% use herbal medication during pregnancy [26, 40].

In 2003, a cross-sectional study was carried out by Jaradat and Sweileh to describe community pharmacy practice in Palestine. They found that OTC sales of many prescription medications were common and unregulated. It also shows that the substitution of prescribed medications was widespread [41]. Another study was conducted by the same authors to determine the sources and needs of drug information for community pharmacies in Palestine. The authors concluded that few information sources were available for community pharmacies, and this was not sufficient for pharmacists to provide patients with appropriate drug information [41].

Pharmacists and nurses in general have a huge role to play in giving information to the public about how best to split or crush OSDFs. To fulfill this aim they should have excellent medication knowledge in all aspects of this subject. The health-care system in Palestine consists of four providers: the Palestinian Ministry of Health (MOH), Palestinian non-governmental organizations (NGOs), the United Nations Relief and Work Agency (UNRWA) and the private sector [42]. The MOH is considered the major provider of primary health services in Palestine. There are 453 primary health-care centers run by the MOH. In addition, the MOH is responsible for a significant portion of the secondary health delivery system's 12 hospitals, which contain 1367 beds [38, 43, 44].

NGOs provide primary and secondary health facilities, such as Red Crescent facilities, Women's Union societies, medical relief committees and Islamic charitable funds [43].Many private medical centers are

operated by private individual specialists, physicians, pharmacists, medical labs and X-ray centers [43]. The final provider for health care is UNRWA. The services are provided to Palestinian refugees and cover medical care, family health, disease control and health education [43].

2.3 Sample size calculation and sampling procedure

In this study the convenience samples of nurses from hospitals and the convenience samples of pharmacists from hospitals and community pharmacies were taken from the visited governorates in the West Bank. Community pharmacies that were closed or in which the pharmacist in charge was not present at the time of the visit were excluded from the study. Hospitals in which the nurse or the pharmacist in charge was not present at the time of the visit were excluded from the study.

The expected number of pharmacists who were licensed by the Palestinian Pharmaceutical Association and working within their field was around 1200, while the expected number of nurses who were licensed by the Palestinian Nurse Association and working in hospitals and connected with splitting or crushing OSDFs was around 800. Based on this, Raosoft software (http://www.raosoft.com/samplesize.html) was used to calculate a suitable sample size and this was 292 for pharmacists and 240 for nurses. In order to minimize erroneous results and increase the study reliability, the target sample size included 300 samples for pharmacists and 250 samples for nurses.

2.4 Data collection instrument

The questions used in the tool had been developed based on previously published studies in other countries. The tool was piloted and tested before the study was officially carried out. The questionnaire used in the tool consists of four sections (Appendix 1 and Appendix 2): section one contained general demographic data such as gender, age, workplace, education, and place and year of graduation. The second section in the tool contained the practical side and consisted of five questions. The first three questions had yes or no answers about practices when crushing or splitting OSDFs; the second two questions, about how often you crush or split OSDFs, gave a choice of the following answers: daily, weekly, monthly or yearly. The final question in this part consisted of a list of many drugs, and the nurses and pharmacists were asked to choose which could be split or crushed. The third section was about measuring attitudes toward splitting or crushing OSDFs and contained nine questions. This section offered the following answers: yes, no, I don’t know. The attitude score ranged from 0 to 9 points. The respondent had a good attitude when the total score ranged from 6 to 9 points and the respondent had a poor attitude when the total score ranged from 0 to 5 points. The fourth section was designed to measure the knowledge of pharmacists and nurses about splitting or crushing OSDFs; it contained 15 questions. The first question in this section concerned the source of information about this subject. The other 14 multiple-choice questions were designed to test information about health-care practitioners; questions in this section had three multiple

choices of which one was correct. We defined the knowledge score as the number of correct answers to the 14 questions that evaluated the participants' knowledge of antibiotic use. The respondent had a good level of knowledge when the total knowledge score ranged from 8 to 14 points and the respondent had a poor knowledge when the total score ranged from 0 to 7 points.The internal consistency and validity of the questionnaire were ensured for the instruments used in our study, namely the Attitude scale (nine items, Cronbach's alpha =0.76) and the Knowledge scale (14 items, Cronbach's alpha =0.73). The tool used in this study had been constructed by the authors and was reviewed and corrected by three PhD holders in clinical and pharmaceutical science that had at least four years of pharmacy practice to ensure content validity.

2.5 Ethical approval

All aspects of the study protocol, including access to and use of the patient clinical information, was obtained from the Institutional Review Board (IRB) at An-Najah National University (Appendix 3) and the required permission from the Palestinian Ministry of Health (Appendix 4). The authors obtained verbal consent from the community pharmacists and nurses who participated in the study.

2.6 Statistical analysis and scoring

Statistical analyses were performed by using the Statistical Package for the Social Sciences (SPSS version 16.0). Mean and standard deviation was

computed for continuous data. Frequencies and percentages were calculated for categorical variables. Data that were not normally distributed were expressed as a median with a range of values (lower-upper quartiles). Data that were not normally distributed were analyzed by the Kruskal-Wallis or Mann-Whitney U test. Variables were tested for normality using the Kolmogorov-Smirnov test. Spearman's correlation coefficient was used to assess whether there was a correlation between variables. Categorical variables were compared using Chi-squared and Fisher's exact tests, as applicable. A p-value of less than 0.05 was considered to be statistically significant for all analyses. Internal consistency was assessed using Cronbach's alpha.

Chapter Three

Results

3. Results

3.1 Demographic characteristics

A total of 615 questionnaires were distributed to the hospitals, community pharmacies and primary health-care centers in Palestine. Sixty-five of the questionnaires were found to be incomplete and were therefore excluded from the analysis. As shown in the summary of demographic characteristics in table 1, the vast majority of the respondents (nurses and pharmacists) were female (72.4% were female and 27.6% were male. More than half of the respondents (nurses and pharmacists) (56.5%) were married. More than half of the respondents (56.9%) were working in hospitals; most of them (89.2%) were nurses and about one-third (34.2%) were working in community pharmacies. The average age of the participants was 32±9.9 years and the average number of years of experience was 8.8±1.8. Two-thirds of the health-care respondents (66.1%) had a bachelor degree, and one-quarter (25.3%) had a diploma most of whom were nurses. Only 8.6% had a master degree, most of whom were pharmacists. The majority of the participants (86.2%) studied at and graduated from local universities. Some of them graduated from Arab universities (10.2%), the others from European (1.3%) and from Turkish, Russian and other universities (2.3%). The distribution of the areas in which respondents were working was as follows: ICU (5.2%), intern (5.2%), surgery (4.8%), delivery (7.4%), neonatal (4.6%), operation (3.1%), emergency (1.5%), women (3.1%), pediatric (1.8%), pharmacy (52.2%), health department (2%), general nurse (2.6%), open heart (1.5%), kidney (0.4%), CCU (1.1%), bone (1.1%). The

specialties of the respondents were as follows: ICU, intern, surgery, general nurse, emergency, neonatal ICU, delivery, pediatric, operation, general pharmacy, kidney, CCU, bone, clinical pharmacy and pharmaceutics. Their percentages are shown in table 1.

Table1. Demographic characteristic of healthcare practitioners

Variable	Total Frequency (%) N=550(100%)	Pharmacists frequency (%) N=300(54.5)	Nurses Frequency (%) N=250(45.5)	P value
Graduation institute				
Local institute	456 (86.2)	226 (79)	230 (94.7)	< 0.001
Arab institute	54 (10.2)	41 (14.3)	13 (5.3)	
Others	19 (3.6)	19 (6.7)	0 (0)	
Marital status				
Married	311 (56.5)	173(57.6)	138 (55.2)	0.451
Single	239 (43.5)	127 (42.3)	112 (44.8)	
Gender				
Male	152 (27.6)	87 (29)	65 (26)	0.433
Female	398 (72.4)	213 (71)	185 (74)	
Place of work				
Hospital	313 (56.9)	90 (30)	223 (89.2)	<0.001
Primary care	48 (8.9)	22 (7.33)	29 (11.6)	
General	188 (34.2)	188 (62.6)	0 (0)	
Pharmacy				
Department				
I.C.U	28 (5.2)	0 (0)	28 (10.9)	<0.001
Intern	28 (5.2)	0 (0)	28 (10.9)	
Surgery	26 (4.8)	0 (0)	26 (10.51)	
Delivery	40 (7.4)	0 (0)	40 (15.6)	
Neonate	25 (4.6)	0 (0)	25 (9.76)	
Operation	17 (3.1)	0 (0)	17 (6.64)	
Emergency	8 (1.5)	0 (0)	8 (3.12)	
Women	17 (3.1)	0 (0)	17 (6.64)	
Pediatric	10 (1.8)	0 (0)	10 (3.9)	
Pharmacy	283 (52.2)	283 (95.3)	0 (0)	
Health	11 (2)	0 (0)	11 (4.29)	
Department	14 (2.6)	0 (0)	14 (5.46)	
General nurse	8 (1.5)	0 (0)	8 (3.12)	
Open heart	2 (0.4)	0 (0)	2 (0.78)	
Kidney	6 (1.1)	12 (4)	18 (7.03)	
CCU	6(1.1)	2 (.67)	4 (1.56)	
Orthopedic				
Age category years				
20-29	309(56.2)	169(56.14)	140(56.2)	<0.001
30-39	131(23.8)	89(29.5)	42(16.86)	
40-49	65(11.8)	19(6.31)	46(18.47)	
50-59	34(6.2)	17(5.64)	17(6.82)	
≥60	11(2)	7(2.32)	4(1.6)	
Educational level				
Diploma	139 (25.3)	0 (0)	139 (55.82)	<0.001
BS	363 (66.1)	261 (87)	102 (40.96)	
MS	47 (8.6)	39 (13)	8 (3.2)	

Variable	Total Frequency (%) N=550(100%)	Pharmacists frequency (%) N=300(54.5)	Nurses Frequency (%) N=250(45.5)	P value
Specialty				
ICU	48 (8.9)	0 (0)	48 (21.2)	
Intern	46 (8.6)	0 (0)	46 (20.3)	
Surgery	20 (3.7)	0 (0)	20 (8.4)	
General nurse	25 (4.6)	0 (0)	25 (10.5)	<0.001
Emergency	13 (2.4)	0 (0)	13 (6.5)	
Neonatal ICU	9 (1.7)	0 (0)	9 (3.8)	
Delivery	35 (6.5)	0 (0)	35 (14.3)	
Pediatric	26 (4.8)	0 (0)	26 (10.9)	
Operation	7 (1.3)	0 (0)	7 (2.9)	
General	281 (52.2)	281 (93.3)	0 (0)	
Pharmacy	2 (.4)	0 (0)	2 (.9)	
Kidney	2 (.4)	0 (0)	2 (.9)	
CCU	2 (.4)	0 (0)	2 (.9)	
Bone	15 (2.8)	15 (5)	0 (0)	
Clinical	4 (.7)	4 (1.3)	0 (0)	
Pharmacy				
Pharmaceutics				
Age				
Mean ±SD	32±9.9	31.97±9.6	32±10.3	<0.001
Experience years				
Mean ±SD	8.8±1.8	8.4±1.9	9.4±1.7	<0.001

3.2 Knowledge of the respondents about crushing or splitting OSDFs

The level of knowledge about crushing or splitting OSDFs, its safety and therapeutic implications was evaluated using statements shown in table 2. When the participants were asked whether extended-release formulations (ER) should not be split or crushed because they are planned for drug release in the intestine not in the stomach, only 20.5% correctly answered no (29.3% of the pharmacists and 10% of the nurses), 52.9% of them answered yes (70.7% of the pharmacists and 31.6% of the nurses), and 26.5% did not know (0% of the pharmacists and 58.4% of the nurses). Among the 550 respondents, 66.4% of them (94.6% of the pharmacists and 32.4% of the nurses) knew that ER formulation consisted of layers or micro

grains with progressive dissolution time. Respondents were less knowledgeable about whether Tegretol 400 mg CR® divitabs can be split or not; only 25.1% (25.7% of the pharmacists and 24.5% of the nurses) agreed with this statement. Only 24.4% of the participants (25% of the pharmacists and 23.6% of the nurses) knew that combination products in the same tablet will not affect the appropriateness for splitting or crushing OSDFs. In fact, 52.7% of the respondents (79.3% of the pharmacists and 20.9% of the nurses) correctly disagreed that Tegretol400 mg CR® divitabs can be crushed. About half of health-care workers (87% of the pharmacists and 15.3% of the nurses) knew that baby aspirin cardio cannot be split because it is enteric coated. In particular, 43.5% (11.8% of the pharmacists and 69.6% of the nurses) did not know that Lescol XL® (fluvastatin) should not be crushed or split because it is extended release. Forty-six of the participants (63.3% of the pharmacists and 27.2% of the nurses) agreed that omeprazole enteric-coated granules should not be crushed because this will inactivate the active ingredients. About 40.7% (62.6% of the pharmacists and 14.4% of the nurses) knew that the administration of crushed nifedipine XL® resulted in increased toxicity. Among the 550 health workers, nearly 40% of them (60.7% of the pharmacists and 15.2% of the nurses) correctly agreed that pancreatin tablet should not be crushed because this will inactivate the active ingredients. About 46.4% of the respondents (29% of the pharmacists and 68% of the nurses) did not know that antineoplastic drugs should not be split or crushed because this will expose health workers to health risks. Respondents were less

knowledgeable about whether nifedipine-coated tablets should not be crushed because the drug is highly light-sensitive; only 19.8% of them (27% of the pharmacists and 11.3% of the nurses) agreed with this statement. Nearly half of the respondents (80.3% of the pharmacists and 26.3% of the nurses) knew that the administration of crushed enteric-coated sulfasalazine tablets led to the release of the drug too early. Finally, only 47 of the participants (74.2% of the pharmacists and 15.3% of the nurses) correctly answered that the administration of crushed alendronate may cause oesophageal irritation.

Table 2 Responses to questions regarding knowledge of health care practitioners toward crushing or splitting Oral solid dosage forms (OSDFs).

Variable	Total frequency (%) N=550 (100%)	Pharmacy frequency (%) N=300 (54.5%)	Nurse Frequency (%) N=250 (45.5%)	P value
K1: Most extended release formulation must not be split or crushed because it is planned for passing the stomach intact and beginning drug release in the intestine:				
Yes	291 (52.9)	212 (70.7)	79 (31.6)	< 0.001
No	113 (20.5)*	88 (29.3)*	25 (10)*	
I do not know	146 (26.5)	0 (0)	146 (58.4)	
K2: Most extended release formulation must not be split or crushed because it is consisting of layers or micro grains with progressive dissolution time:				
Yes	365 (66.4)*	284(94.6)*	81 (32.4)*	<0.001
No	34 (6.2)	8 (2.7)	26 (10.4)	
I don't know	151 (27.5)	8 (2.7)	143 (57.2)	
K3: Tegretol 400 mg CR® (carbamzepine, Novartis company) Divitabs can be split?				
Yes	138 (25.1)*	77 (25.7)*	61 (24.5)*	<0.001
No	253 (46)	197 (65.7)	56 (22.5)	
I do not know	158 (28.7)	26 (8.7)	132 (53)	
K4: If tablet contains a combination product; this will not affect the appropriateness or recommending for splitting or crushing or not?				
Yes	134 (24.4)*	75 (25)*	59 (23.6)*	<0.001
No	267 (48.5)	190(63.3)	77 (30.8)	
I don't know	149 (27.1)	35 (11.7)	114 (45.6)	
K5: Tegretol 400 mg CR® (carbamzepine, Novartis companyDivitabs) can be crushed?				
Yes	55 (10)	14 (4.7)	41 (16.5)	<0.001
No	290 (52.7)*	238(79.3)*	52 (20.9)*	
I don't know	(37.1)	48 (16)	156 (62.6)	
K6: Baby Aspirin cardio® (acetyl salicylic acid, Bayer company) cannot be split or crushed because it is				
Enteric coated	299 (54.4)*	261(87)*	38 (15.3)*	<0.001
Extended release	80 (14.5)	17 (5.7)	63 (25.3)	
I don’t know	170 (30)	22 (7.3)	148 (59.4)	

K7: Lescol XL® (fluvastatin, Novartis company) should not be split or crushed because it is				<0.001
Enteric coated	50 (9.1)	25 (4.5)	25 (10)	
Extended release	261 (47.5)*	210(38.2)*	51 (20.4)*	
I don't know	239 (43.5)	65 (11.8)	174 (69.6)	
K8: Omeprazole enteric coated granule should not be crushed or split because this will:				<0.001
Increase Toxicity	104 (18.9)	75 (25)	29 (11.6)	
Inactivate active ingredient	258 (46.9)*	190(63.3)*	68 (27.2)*	
I don't know	188 (34.2)	35 (11.7)	153(61.2)	
K9: The administration of a crushed nifedipine XL tablet resulted in				<0.001
Increase Toxicity	224 (40.7)*	188(62.6)*	36 (14.4)*	
Inactivate active ingredient	87 (15.8)	49 (16.3)	38 (15.2)	
I don't know	239 (43.5)	63 (21)	176 (70.4)	
K10: Pancreatin tablet should not be split or crushed because this will				<0.001
Increase Toxicity	76 (13.8)	46 (15.3)	30 (12)	
Inactivate active ingredient	220 (40)*	182(60.7)*	38 (15.2)*	
I don't know	254 (46.2)	72 (24)	182 (72.8)	
K11: Antineoplastic agent should not be split or crushed because:				<0.001
This will inactivate active ingredient	64 (11.6)	46 (15.4)	18 (7.3)	
These agents may expose carers or health care professionals to health risks	227 (41.3)*	166(55.5)*	61 (24.7)*	
I don't know	255 (46.4)	87 (29)	168 (68)	
K12: Nefidipne coated tablet should not be crushed because				<0.001
The drug is highly light sensitive	109(19.8)*	81 (27)*	28(11.3)*	
Increase conc. and toxicity	190 (34.5)	133 (44.5)	57 (23)	
I don't know	247 (44.9)	85 (28.4%)	162(65.5)	
K13: The administration of a split or crushed enteric coated sulphasalazine tablet resulted in				<0.001
Increase the conc. and toxicity	36 (6.5)	20 (6.7)	16 (6.5)	
The drug is being release too early	306(55.6)*	241(80.3)*	65(26.3)*	
I don't know	205 (37.3)	39 (13)	166(67.2)	
K14: Alendronate drug should not be crushed because				<0.001
This will inactivate active ingredient	68 (12.4)	32 (10.7)	36 (14.5)	
Due to risk of esophageal irritation	259(47.1)*	221(74.2)*	38(15.3)*	
I don't know	219 (39.8)	45 (15.1)	174 (70)	

*was used for correct answer

3.3 Attitudes of the respondents toward crushing or splitting OSDFs

Data on respondents' attitude toward crushing or splitting OSDFs are found in table 3.In general, 26.7% of the participants (28.3% of the pharmacists and 24.9% of the nurses) thought that splitting tablets is a useful way to reduce medication costs. In response to the question of whether physicians should prescribe split tablets as often as possible to reduce medication costs, the viewpoint of almost 79% of the respondents (90.7% of the pharmacists and 65% of the nurses) disagreed with this idea. Most (88%) of the respondents (95.6% of the pharmacists and 78.8% of the nurses) agreed that sometimes it is difficult to break tablets because they are small or hard. An 82% positive response was reported by participants (93.7% of the pharmacists and 69.2% of the nurses) when they were asked whether sometimes even scored tablets cannot be divided into equal parts. Only 20.8% of the respondents (3.5% of the pharmacists and 17.3% of the nurses) supported the idea that all tablets can be split or crushed if required. Nearly 56% of respondents (61.2% of the pharmacists and 50% of the nurses) agreed that sometimes they are not sure whether tablets are indeed suitable for splitting or crushing. With regard to the information about splitting or crushing OSDFs, 49.1% of the respondents (44% of the pharmacists and 55.2% of the nurses) expect to find information about this in the package leaflets. Fifty-five percent of health workers in this study didn't ask experts about how to split tablets best. Finally, over 56% of participants (57.6% of the pharmacists and 56% of the nurses) thought that splitting or crushing OSDFs is part of the doctor's role or responsibility.

Table 3 Responses to questions regarding attitudes of health care practitioners toward crushing or splitting Oral solid dosage forms (OSDFs).

Variable	Total Frequency (%) N=550(100%)	Pharmacy Frequency (%) N=300(54.5%	Nurse Frequency (%) N=250(45.5%)	P value
A1: Tablet splitting is a useful way to reduce medication costs				
Yes	147 (26.7)	85 (28.3)	62 (24.9)	<0.001
No	342 (62.2)®	203 (67.7)®	139 (55.8)®	
I don't know	60 (10.9)	12 (4)	48 (19.3)	
A2: To reduce medication costs physician should prescribe split tablets as often as possible.				
Yes	46 (8.4)	15 (5)	31 (12.5)	<0.001
No	435 (79.1)®	272 (90.7)®	163 (65)®	
I don't know	69 (12.5)	13 (4.3)	56 (22.5)	
A3: Sometimes it is difficult to break tablets (e.g. because they are very small or hard)				
Yes	483 (88)+	286 (95.6)+	197 (78.8)+	<0.001
No	31 (5.6)	4 (1.3)	27 (10.8)	
I don't know	35 (6.4)	9 (3.1)	26 (10.4)	
A4: Sometimes even scored tablets cannot be divided into equal part				
Yes	454 (82.5)+	281 (93.7)+	173 (69.2)+	<0.001
No	71 (12.9)	16 (5.3)	55 (22)	
I don't know	25 (4.5)	3 (1)	22 (8.8)	
A5: If required, all tablets may be split or crushed				
Yes	114 (20.8)	19 (3.5)	95 (17.3)	<0.001
No	366 (66.7)®	266 (48.5)®	100 (18.2)®	
I don't know	69 (12.6)	15 (2.7)	54 (9.8)	
A6: Sometimes I am not sure whether tablets are indeed suitable for splitting or crushing.				
Yes	308 (56)	183 (61.2)	125 (50)	<0.001
No	187 (34)®	101(33.8)®	86(34.4)®	
I don't know	54 (9.8)	15 (5)	39 (15.6)	
A7: If tablets are not suitable for splitting or crushing I expect to find this information in the package leaflet.				
Yes	270 (49.1)	132 (44)	138 (55.2)	<0.001
No	223 (40.5)	158 (52.7)	65 (26)	
I don't know	57 (10.4)	10 (3.3)	47 (18.8)	

A8: I have ever been asked expert on how to split tablets best				
Yes	306 (55.6)	172 (57.3)	134 (53.6)	0.294
No	170 (30.9)®	99 (33)®	71(28.4)®	
I don't know	74 (13.5)	29 (10)	45 (18)	
A9: I think that modifying the dosage form is part of the doctors role or responsibility				
Yes	313 (56.9)	173 (57.6)	140 (56)	0.695
No	193 (35.1)	107 (35.6)	86 (34.4)	
I don't know	44 (8)	20 (6.7)	24 (9.6)	

® was used for correct negative answer

+ was used for correct positive answer

3.4 Practices of the respondents toward crushing or splitting OSDFs

Data on respondents' practice toward crushing or splitting OSDFs are found in table 4. In general, around 35% of the health workers (15% of the pharmacists and 85.8% of the nurses) in the study had split or crushed enteric-coated or sustained-release OSDFs such as baby aspirin cardio, Tegretol CR®, Pentasa® etc. Around 93.5% of the respondents (95.3% of the pharmacists and 91.2% of the nurses) didn't receive training in drug stability after splitting or crushing OSDFs. As far as encouraging pill splitting as a way to help patients save money is concerned, 20% of the participants (14.7% of the pharmacists and 26.8% of the nurses) agreed with this statement. When the participants were asked how often they split tablets as a way to obtain the desired dose, only 17% of them answered daily, 18% weekly, 30.9% monthly and 33% didn't split tablets. Finally, when the participants were asked how often they crushed tablets, only 13% of them answered daily, 7% weekly, 18% monthly and 62% didn't crush tablets.

Table 4: Responses to questions regarding practices of health care practitioners toward crushing or splitting Oral solid dosage forms (OSDFs).

Variable	Total Frequency (%) N=550 (100%)	Pharmacists Frequency (%) N=300 (54.5%)	Nurses Frequency (%) N=250 (45.5%)	p-value
P1:Have you encourage pill splitting as a way to help patient save money				<0.001
Yes	111 (20.2)	44 (14.7)	67 (26.8)	
No	439 (79.8)	256 (85.3)	183 (73.2)	
P2: Have you split or crush enteric coated tablet like Baby aspirin or sustained release like (TegretolCR AdizemCD,Osmo-Adalat, Pentasa) ®?				
Yes	195 (35.5)	48 (15)	147 (85.8)	<0.001
No	355 (64.5)	252 (85)	103 (41.2)	
P3: Have you received training in drug stability after splitting or crushing OSDFs?				
Yes	36 (6.5%)	14 (4.7%)	22 (8.8%)	<0.001
No	514 (93.5%)	286 (95.3%)	228 (91.2%)	
P4: How often have you split tablets as a way to reach the desired dose?				<0.001
Daily	94 (17.1)	23 (7.7)	71 (28.4)	
Weekly	101 (18.4)	78 (26)	23 (9.2)	
Monthly	170 (30.9)	118 (39.3)	52 (20.8)	
Non	185 (33.6)	81 (27)	104 (41.6)	
P5: How often have you done tablet crushing?				
Daily	72 (13.1)	11 (3.6)	61 (24.4)	<0.001
Weekly	38 (6.9)	13 (4.3)	25 (10)	
Monthly	100 (18.2)	67 (22.3)	33 (13.2)	
Non	340 (61.8)	209 (69.6)	131 (52.4)	

3.5 Knowledge, attitude and practice scores among pharmacists

The reported knowledge score as measured by mean scores value and attitude score was 8.7 ± 2.7 and 6.4 ± 1.4, respectively. There was a significant modest positive correlation (r=0.18, p=0.002) between the attitude and knowledge scores. The reported attitude score as measured by mean score value for practice respondents (i.e. who crushed or split OSDFs) was 6.3 ±1.4 vs. 6.3 ± 1.4 for non-practice. There was no significant difference between practice and non-practice respondents

regarding attitude score (p-value 0.67).The reported knowledge score as measured by mean score value for practice respondents was 9.4 ±2.9 vs. 8.6 ±2.6 for non-practice. There was a significant difference between practice and non-practice respondents regarding knowledge score (p=0.037).

3.5.1 Knowledge score among pharmacists

The median knowledge score among pharmacists was 9 (interquartile range: 7–11). Nearly two-thirds of respondents (67.3%) had a good level of knowledge (a total knowledge score 8–14) and 32.7% of respondents had a poor level of knowledge.

As shown in table 5, a significant difference in the knowledge of pharmacists toward crushing or splitting OSDFs was found among participant groups according to age only (Kruskal-Wallis test; $p<0.05$). There was no significant association between the six demographic variables of marital status, gender, education level (Mann-Whitney test, $p>0.05$), graduation institute, place of work and specialty (Kruskal-Wallis test; $p>0.05$) and the knowledge of pharmacists about crushing or splitting OSDFs. Pharmacists aged more than 60 years old were associated with a high median index value, but patients aged from 50 to 59 years had a lower median value.

Table 5: Association of Socio-demographic with pharmacists knowledge score total scores

Variable	Pharmacists Frequency (%) N=300	Knowledge score Median (interquartile range)	p- value
Graduation institute			
Local institute	226 (79)	10(7-11)	
Arab institute	41 (14.3)	8(7-10)	0.096
Others	19 (6.7)	9(6-10)	
Marital status			
Married	173(57.6)	10(7-11)	0.590
Single	127 (43.3)	9(7-11)	
Gender			
Male	87 (29)	10(7-11)	0.441
female	213 (71)	9(7-11)	
Place of work			
Hospital	90 (30)	10(6-11	0.382
Primary care	22 (7.33)	8(7-10)	
General pharmacy	188 (62.6)	9(7-11)	
Age category Years			
20-29	169(56.14)	10(7-11)	0.048
30-39	89(29.5)	9(7-10)	
40-49	19(6.31)	10(6-10)	
50-59	17(5.64)	8(5-9)	
≥60	7(2.32)	11(6-11)	
Educational level			
BS	261 (87)	9(7-11)	0.551
MS	39 (13)	10(7-11)	
Specialty			
General pharmacy	281 (93.3)	9(7-11)	
Clinical pharmacy	15 (5)	10(9-11)	
Pharmaceutics	4 1.3)	10(7.75-11.5)	0.468

3.5.2 Attitude scores among pharmacists

The median attitude score among pharmacists was 6 (interquartile range: 5–7). More than two-thirds of pharmacists (69%) had a good attitude (a

total score of 6–9 points) and 31% of pharmacists had a poor attitude (a total score of 0–5). As shown in table 6, a significant difference in the attitudes of pharmacists toward crushing or splitting OSDFs was found among participant groups according to specialty only (Kruskal-Wallis test; $p<0.05$) There was no significant association between the six demographic variables (marital status, gender, education level (Mann-Whitney test, $p>0.05$), graduation institute, age and place of work (Kruskal-Wallis test; $p>0.05$) and the attitudes of pharmacists toward crushing or splitting OSDFs. Pharmaceutics specialist pharmacists were associated with a higher median index value than general and clinical pharmacists.

Table 6 Association of Socio-demographic with pharmacists Attitudes score total scores

Variable	Pharmacists Frequency (%) N=300	Attitudes score Median (interquartile range)	P value
Graduation institute			
Local institute	226 (79)	6(5-7)	0.149
Arab institute	41 (14.3)	7(6-8)	
Others	19 (6.7)	6(5-8)	
Marital status			
Married	173 (57.6)	6(5-8)	0.554
Single	127 (42.3)	6(5-7)	
Gender			
Male	87 (29)	6(5-8)	0.931
Female	213 (71%)	6(5-7)	
Place of work			
Hospital	90 (30)	6(5-8)	0.807
Primary care	22 (7.33)	6(5-7)	
General pharmacy	188 (62.6)	6(5-7)	
Age category			
20-29	169(56.14)	6(5-7)	0.165
30-39	89(29.5)	7(5-8)	
40-49	19(6.31)	7(5-7)	
50-59	17(5.64)	6(5-8)	
≥60	7(2.32)	6(5-7)	
Educational level			
BS	261 (87)	6(5-7)	
MS	39 (13)	6(5-8)	0.281
Specialty			
General pharmacy	281 (93.3)	6(5-7)	0.004
Clinical pharmacy	15 (5)	5(5-6)	
Pharmaceutics	4 1.3)	8(7.25-8.75)	

3.5.3 Practices among pharmacists

The number of pharmacists with good practice who didn't crush or split enteric-coated or sustained-release OSDFs was 251 (83.7%). As shown in table 7, a significant difference in the practice of pharmacists toward crushing or splitting enteric-coated or sustained-release OSDFs was found among participant groups according to age only ($p<0.05$). There was no significant association between the six demographic variables (marital status, gender, education level, graduation institute, specialty and place of

work (p>0.05) and the practice of pharmacists toward crushing or splitting enteric-coated or sustained-release OSDFs. The study found that the age category from 20 to 29 years was associated with the highest frequency of good practice value among pharmacists.

Table 7 :Association of Socio-demographic with pharmacists practice frequency total scores

Variable	Yes Frequency (%)	No Frequency (%)	Total Pharmacy Frequency N=300 (%)	P value
Graduation institute				
Local institute	42(85.7)	184(77.6)	226(79)	0.076
Arab institute	7(14.3)	34(14.3)	41(14.3)	
Others	0(0)	19(8)	19(6.6)	
Marital status				
Married	28(57.1)	146(58.2)	174(58)	0.894
Single	21(42.9)	105(41.8)	126(42)	
Gender				
Male	15(30.6)	72(28.7)	87(29)	0.786
female	34(69.4%)	179(71.3)	213(71)	
Place of work				
Hospital	14(28.6)	77(30.7)	91(30.3)	0.773
Primary care	7(14.3)	15(6)	22(7.3)	
General pharmacy	28(57.1)	159(63.3)	187(62.3)	
Age category				
20-29	34(69.4)	134(53.4)	168(56)	0.03
30-39	15(30.6)	74(29.5)	89(29.7)	
40-49	0(0)	19(7.6)	19(6.3)	
50-59	0(0)	17(6.8)	17(5.7)	
≥60	0(0)	7(2.8)	7(2.3)	
Educational level				
BS	45(91.8)	216(86.1)	261(87)	0.272
MS	4(8.2)	35(13.9)	39(13)	
Specialty				
General pharmacy	47(95.5)	234(93.2)	281(93.7)	0.903
Clinical pharmacy	0(0)	15(6)	15(5)	
Pharmaceutics	2(4.1)	2(0.8)	4(1.3)	

3.6 Knowledge, attitude and practice scores among nurses

The reported knowledge score as measured by mean scores value and attitude score was 2.9 ± 2.7 and 4.8 ± 1.9, respectively. There was a significant modest positive correlation (r=0.24, p<0.001) between the

attitude score and knowledge score. The reported attitude score as measured by mean score value for practice respondents was 4.7 ±1.7 vs. 4.9 ±2.2 for non-practice. There was no significant difference between practice and non-practice respondents regarding attitude score (p=0.46). The reported knowledge score as measured by mean score value for practice respondents was 3.2 ±2.8 vs. 2.5 ±2.5 for non-practice. There were slight differences between practice and non-practice respondents regarding knowledge score (p=0.047).

3.6.1 Knowledge score among nurses

The median knowledge score among nurses was 2 (interquartile range: 0.75–5). Only 5.6% of nurses had a good level of knowledge (a total knowledge score of 8–14) and most nurses (94.4%) had a poor level of knowledge (a total knowledge score of 0–7).

As shown in table 8, a significant difference in the knowledge of nurses about crushing or splitting OSDFs was found among participant groups according to gender, marital status (Mann-Whitney test, $p<0.05$), education level and specialty (Kruskal-Wallis test; $p<0.05$). There was no significant association between the four demographic variables of graduation institute, place of work (Mann-Whitney test, $p>0.05$), department and age (Kruskal-Wallis test; $p>0.05$) and the knowledge of nurses about crushing or splitting OSDFs. The study found that married nurses had a higher median index value than single ones. Furthermore, the male gender was associated with a higher median index value than the female gender. It also found that

nurses with a master degree were more likely to have a better knowledge of crushing or splitting OSDFs than others. However, there was a strong association between the specialty of nurses and knowledge score; I.C.U., emergency and delivery nurses were associated with a high knowledge score.

Table 8 : Association of Socio-demographic with Nurses knowledge score total scores (N=14)

Variable	Nurse Frequency (%) N=250	Knowledge score Median (interquartile range)	P value
Graduation institute			
Local institute	230 (94.7)	2(1-5)	0.162
Arab institute	13 (5.3)	0(0-5)	
Marital status			
Married	138 (55.2)	3(1-5)	0.002
Single	112 (44.8)	1(0-4)	
Gender			
Male	65 (26)	4(1-6)	<0.001
female	185 (74)	2(0-4)	
Place of work			
Hospital	223 (89.2)	2(0-5)	0.876
Primary care	29 (11.6)	2(1-5)	
Department			
I.C.U	28 (10.9)	4(1-6)	0.313
Intern	28 (10.9)	1(0-5.75)	
surgery	26 (10.51)	2(0-4)	
Delivery	40 (15.6)	3(1-4)	
Neonate	25 (9.76)	1(0.5-3.5)	
Operation	17 (6.64)	390-6.5)	
Emergency	8 (3.12)	4(0.25-6.75)	
Women	17 (6.64)	1(1-5.5)	
Pediatric	10 (3.9)	2(0-7)	
Health department	11 (4.29)	1(0-5)	
General nurse	14 (5.46)	2(0-4)	
Open heart	8 (3.12)	3(2-5.75)	
CCU	24(9.3)	5(0-7)	
Age category years			
20-29	140(56.2)	2(1-5)	0.088
30-39	42(16.86)	4(0-6)	
40-49	46(18.47)	2(0-4.25)	
50-59	17(6.82)	1(0-2)	
≥60	4(1.6)	5(3-7)	
Educational level			
Diploma	139 (55.82)	4(2-7)	0.024
BS	102 (40.96)	2.5(1-6)	
MS	8 (3.2)	5.5(4-6)	

Specialty			
ICU	48 (21.2)	4(1-6)	0.004
Intern	46 (20.3)	1.5(0-5)	
Surgery	20 (8.4)	0(0-3.75)	
General nurse	25 (10.5)	2(1-4)	
Emergency	13 (6.5)	4(1-5)	
Neonatal ICU	9 (3.8)	1(0-3)	
Delivery	35 (14.3)	4(1.75-6)	
Pediatric	26 (10.9)	1.5(1-3.25)	
Operation	7 (2.9)	0(0-6)	
Orthopedic	6(2.1)	3(0-7)	

3.6.2 Attitude score among nurses

The median attitude score among nurses was 4 (interquartile range: 4–6)**.** Only 36.4% of nurses had a good attitude (a total score of 6–9 points) and 63.6% of nurses had a poor attitude (a total score of 0–5 points).

As shown in table 9, a significant difference in the attitudes of nurses toward crushing or splitting OSDFs was found among participant groups according to marital status (Mann-Whitney test, $p<0.05$), education level and speciality (Kruskal-Wallis test; $p<0.05$). There was no significant association between the five demographic variables of graduation institute, place of work, gender (Mann-Whitney test, $p>0.05$), department and age (Kruskal-Wallis test; $p>0.05$) and the attitudes of nurses toward crushing or splitting OSDFs. The study found that married nurses had a higher median index value than single ones. It also found that bachelors and nurses with a master degree were more likely to have a better knowledge of crushing or splitting OSDFs than those with a diploma, however there was a strong association between the specialty of nurses and attitudes score. Bone nurses were associated with the highest knowledge score, followed by pediatric, delivery, emergency, I.C.U. and general nurses.

Table 9 Association of socio-demographic with nurses attitudes score total scores

Variable	Nurse Frequency (%) N=250	Attitudes score Median (interquartile range)	P value
Graduation institute			
Local institute	230 (94.7)	5(4-6)	0.317
Arab institute	13 (5.3)	5(4-6)	
Marital status			
Married	138 (55.2)	5(4-6)	0.010
Single	112 (44.8)	4(3-6)	
Gender			
Male	65 (26)	5(3-6.5)	0.520
Female	185 (74)	5(4-6)	
Place of work			
Hospital	223 (89.2)	5(4-6)	
Primary care	29 (11.6)	6(4-6)	>0.05
Department			
I.C.U	28 (10.9)	6(4-7)	
Intern	28 (10.9)	4(3-6)	
surgery	26 (10.51)	4(2-5)	0.007
Delivery	40 (15.6)	5(4-6)	
Neonate	25 (9.76)	4(4-6)	
Operation	17 (6.64)	5(4-6.5)	
Emergency	8 (3.12)	6.5(3.75-7.75)	
Women	17 (6.64)	5(3.5-6.5)	
Pediatric	10 (3.9)	5(3-5)	
Health department	11 (4.29)	5(4-6)	
General nurse	14 (5.46)	4.5(3.75-6)	
Open heart	8 (3.12)	3.5(3-5.5)	
CCU	24(9.3)	5.5(5-6)	
Age category years			
20-29	140(56.2)	5(4-6)	
30-39	42(16.86)	5(3-6)	0.717
40-49	46(18.47)	5(4-6)	
50-59	17(6.82)	5(4-6)	
≥60	4(1.6)	5.5(2-6)	
Educational level			
Diploma	139 (55.82)	4(3-6)	<0.001
BS	102 (40.96)	5(4-7)	
MS	8 (3.2)	4.5(3.25-6.75)	
Specialty			
ICU	48 (21.2)	5(4-6)	
Intern	46 (20.3)	4(3-6)	
Surgery	20 (8.4)	4(2-5)	<0.001
General nurse	25 (10.5)	5(4-6)	
Emergency	13 (6.5)	5(4-7)	
Neonatal ICU	9 (3.8)	4(3-6)	
Delivery	35 (14.3)	5(4-6)	
Pediatric	26 (10.9)	5(4-6.25)	
Operation	7 (2.9)	2(0-5)	
Orthopedic	6(2.1)	7(5-7.25)	

3.6.3 Practice score among nurses

The number of nurses with good practice who didn't crush or split enteric-coated or sustained-release OSDFs was 104(41.6%). As shown in table 10, a significant difference in the practice of nurses toward crushing or splitting enteric-coated or sustained-release OSDFs was found among participant groups according to gender, department, place of work, age and specialty ($p<0.05$). There was no significant association between the three demographic variables of marital status, graduation institute ($p>0.05$) and education level ($p>0.05$) and the practice of nurses toward crushing or splitting enteric-coated or sustained-release OSDFs. The study found that female nurses were associated with a better practice frequency value than male nurses.

Table 10: Association of socio-demographic with nurses practice score total scores

Variable	Yes Frequency (%)	No Frequency (%)	Total Nurse Frequency (%) N=250	P value
Graduation institute				
Local institute	137(95.8)	93(93.8)	230(94.7)	0.340
Arab institute	6(4.2)	7(7)	13(5.3)	
Marital status				
Married	79(54.1)	58(55.8)	137(54.8)	0.795
Single	67(45.9)	46(44.2)	113(45.2)	
Gender				
Male	52(35.6%)	13(12.5)	65(26)	<0.001
female	94(64.4%)	91(87.5)	185(74)	
Place of work				
Hospital	137(93.8)	85(81.7)	222(88.8)	0.03
Primary care	9(6.2)	19(18.3)	28(11.2)	
Department				
I.C.U	20(14.1)	8(0.8)	28(11.6)	
Intern	18(12.7)	10(10)	28(11.6)	
Surgery	22(15.5)	4(4)	26(10.7)	0.012
Delivery	21(14.8)	19(19)	40(16.5)	
Neonate	15(10.6)	10(10)	25(10.3)	
Operation	6(4.2)	11(11)	17(7)	
Emergency	4(2.8)	4(4)	8(3.3)	
Women	10(7)	7(7)	17(7)	
Pediatric	8(5.6)	3(3)	11(4.5)	
Health Department	1(.7)	10(10)	11(4.5)	
General Nurse	9(6.3)	5(5)	14(5.8)	
Open heart	4(2.8)	4(4)	8(3.3)	
CCU	4(2.8)	5(5)	9(3.7)	
Age category Years				
20-29	89(61)	52(50)	141(56.4)	
30-39	26(17.8)	16(15.4)	42(16.8)	0.019
40-49	22(15.1)	24(23.1)	46(18.4)	
50-59	8(5.5)	9(8.7)	17(6.8)	
≥60	1(0.7)	3(2.9)	4(1.6)	
Educational level				
Diploma	84(57.5)	55(53.4)	139(55.8)	0.785
BS	56(38.4)	46(44.7)	102(41)	
MS	6(4.1)	2(1.9)	8(3.2)	
Specialty				
ICU	34(23.9)	14(14.6)	48(20.2)	
Intern	26(18.3)	20(20.8)	46(19.3)	
Surgery	18(12.7)	2(2.1)	20(8.4)	0.01
General nurse	13(9.2)	12(12.5)	25(10.5)	
Emergency	8(5.6)	5(5.2)	13(5.5)	
Neonatal ICU	4(2.8)	5(5.2)	9(3.8)	
Delivery	17(12)	17(17.7)	34(14.3)	
Pediatric	17(12)	9(9.4)	26(10.9)	
Operation	4(2.8)	7(7.3)	11(4.6)	
bone	1(0.7)	5(5.2)	6(2.5)	

Chapter Four

Discussion

4. Discussion

This study identifies the current knowledge, attitudes and practice of health-care practitioners regarding splitting or crushing OSDFs and awareness about its safety and therapeutic implications. It also identifies the demographic characteristics associated with particular knowledge, attitudes and practices and highlights the gaps in public knowledge about this subject.

Previous related studies on the same subject in the region were not available or found. In fact, to our knowledge this study is the first one to be conducted in our region. This study was conducted among 550 health-care practitioners (nurses and pharmacists) to investigate their knowledge, attitudes and practices regarding splitting or crushing OSDFs.

The study results revealed that the vast majority of the respondents (nurses and pharmacists) were female (72.4% were female and 27.6% were male).This is compatible with the statistics of the Palestinian Ministry of Health (2008), which estimated that most of the nurses and pharmacists in the West Bank were females. More than half of the respondents (nurses and pharmacists) (56.5%) were married. More than half of the respondents (56.9%) were working in hospitals; most of them (40.5%) were nurses and about one-third (34.2%) were working in community pharmacies. This is due to governmental hospital needs to employ nurses more than pharmacists as opposed to the needs of pharmacies. The average age of the participants was 32±9.9 years, the average number of years of experience

was 8.8±9.1 and most of the participants were from the age group 20–29 years; this might be due to the presence and launching of new faculties in Palestine for pharmacists and nurses. Two-thirds of the health-care respondents (66.1%) had a bachelor degree, one-quarter (25.3%) had a diploma most of whom were nurses, and only 8.6% had a master degree, most of whom were pharmacists. The majority of the participants (86.2%) studied at and graduated from local universities; some of them (10.2%) graduated from Arab universities, the others studied at other countries (1.3%).

4.1 Knowledge of health-care practitioners

The questions that were addressed in this section aimed to measure the level of knowledge of health-care workers about splitting or crushing OSDFs, to assess whether they knew the effect of drug dosage form on its suitability for being split or crushed, and to discover whether they understood what occurred when some classes of drugs or dosage forms such as antineoplastic drugs were split or crushed.

The results were as follows: nearly two-thirds of pharmacists (67.3%) had a good level of knowledge (a total knowledge score of 8–14) and 32.7% of them had a poor level of knowledge, while only 5.6% of nurses had a good level of knowledge and most nurses (94.4%) had a poor level of knowledge. This result can be justified since the curriculum of pharmacy include courses that focuses on pharmaceutical technology which deals with MR dosage forms while nurses do not have such topics in their

courriculm. These results are fairly close to the results of some studies regarding nurses. Mafiana et al. [45] found that there was a knowledge deficit regarding special formulations that should not be crushed among nurses, while another study conducted by Dashti-Khavidaki et al. [46] found that more than half of nurses had insufficient knowledge about the characteristics of dosage forms. We didn't find any study similar to ours regarding the knowledge of pharmacists, thus we are unable to discuss this in the light of other results. However, studies performed among different subjects, such as a study in the UK that was conducted to investigate the knowledge of UK hospital pharmacists regarding adverse drug reaction reporting, showed that pharmacists have a reasonable knowledge about spontaneous adverse drug reaction reporting schemes [47].

Out of 550 respondents, 66.4% of them knew that ER formulation consisted of layers or micro grains with progressive dissolution time, but only 20% of the respondents could differentiate between extended-release and enteric-coated preparations. However, a study conducted by Mafiana et al. [45] found that only 38% of nurses could correctly indicate how they would recognize sustained formulations. This showed that there is a shortage of ongoing education after graduation. On the other hand, the respondents were not well informed about the effect of more than one active ingredient in the same tablet on splitting OSDFs: only 24.4% of the participants knew that combination products in the same tablet will not affect the appropriateness for splitting or crushing OSDFs. Respondents were less knowledgeable about whether nifedipine-coated tablets should

not be crushed because the drug is highly light-sensitive, which may have a negative impact on drug stability. This is very dangerous because most health workers are not aware of this problem. Among health-care practitioners, most nurses (in contrast to pharmacists) were not knowledgeable about the changes that happen when crushing or splitting Tegretol® 400 mg GR, Lescol XL®, omeprazole enteric-coated granules, nifedipine XL®, pancreatin tablets and antineoplastic drugs. This is a cause for concern because many studies have shown that adverse reactions and death have occurred due to changes in the physical characteristics of some of these drugs. Schier et al. [24] gave an example of a case of the death of a patient due to the administration of crushed controlled-release nifedipine with labetalol. The administration of crushed controlled-release nifedipine resulted in severe patient hypotension, and the concurrent administration of labetalol prevented a compensatory heart rate increase and this led to death [24]. Only 20.9% of nurses knew that Tegretol® 400 mg CR can be crushed compared with 79.3% of pharmacists who knew this. In another example, 27.2% of nurses agreed that omeprazole enteric-coated granules should not be crushed because this will inactivate the active ingredient compared with 63.3% of pharmacists who knew this. However, a study by Cornish reported on death as a result of respiratory depression in a patient due to the administration of crushed sustained-release codeine in addition to the loss of efficacy of crushed enteric-coated omeprazole [11]. According to our study, in addition to these findings from literature there is a need for the scope in teaching to improve nurses' knowledge in this

respect. Additionally, these results indicate the need of presence of pharmacists (clinical pharmacists or pharmacy Doctors) during the morning round at hospital or at least they should be consulted for such issues.

4.2 Attitudes of health-care practitioners

The median attitude score among pharmacists was 6. More than two-thirds of pharmacists had a good attitude and 31% of pharmacists had a poor attitude. Meanwhile the median attitude score among nurses was 4. Only 36.4% of nurses had a good attitude and 63.6% of nurses had a poor attitude. With regard to the attitude of health-care practitioners, it was found that pharmacists had a better attitude (69%) than nurses (36.4%). These results are similar to knowledge results for nurses and pharmacists. We didn't find any study similar to ours among nurses and pharmacists, thus we are unable to discuss this in the light of other results. However, studies were performed among different subjects, such as a study in India that was conducted to measure the knowledge, attitudes and practices of pharmacists regarding adverse drug reaction, as well as another study in Iran among nurses measuring the same things. The findings of these studies showed that Iranian nurse attitudes toward adverse drug reaction reporting was at a high level, while Indian pharmacists have poor attitudes [48, 49].

Table 3,which summarizes the responses received as regards the attitudes to splitting or crushing OSDFs of health-care practitioners, illustrates that two-thirds or more of them agree that tablet splitting is not a useful way to reduce medication costs, don't believe that physicians should prescribe

split tablets as often as possible to reduce medication costs, believe that sometimes it is difficult to break tablets because they are small or hard, and that sometimes even scored tablets cannot be split into two equal parts, and don’t think that all tablets can be split if required. A study conducted by Quinzler et al. [29] showed that splitting tablets in primary care centers is a frequent event due to economic considerations. In the same study nearly 1% of all tablets that were divided could not be fragmented or disintegrated.

Nearly half of the participants agreed that they are not sure whether tablets are indeed suitable for splitting or crushing, that they have never asked an expert how to split tablets best, and that they expect to find information in the package leaflet if tablets are not suitable for splitting or crushing. A study conducted by Al-Ramahi et al. [50] to explore the attitude of the Palestinian public and health-care professionals towards patient package inserts (PPIs) found that a high percentage of consumers always read the PPIs. Authors also found that 74.0% of consumers and 83.7% of health-care professionals said that the information in the PPIs needs to be improved. It is clear that drug companies should improve the pharmacological and pharmaceutical contents in PPIs [50]. In fact, these recommendations may be useful in this regard, since it may be helpful for patients and healthcare providers about right way to conduct this practice.

4.3 Practices of health-care practitioners

Questions that were addressed in this section aimed to measure levels of good practice of health-care workers regarding splitting or crushing OSDFs, to assess whether they received training in drug stability, and to discover how often they have split or crushed OSDFs, especially enteric-coated and extended-release dosage forms.

The responses were as follows: in general, around 35% of the health workers (15% of the pharmacists and 85.8% of the nurses) have split or crushed enteric-coated or sustained-release OSDFs, which means that most nurses used this wrong practice in contrast to pharmacists, and this may be the result of the lack of knowledge among nurses or as a result of physician orders. We didn't find any study similar to ours among nurses and pharmacists, thus we are unable to discuss this in the light of other results. A retrospective cohort study by Chia-yu et al. [36] found that there were 1252 incidents of inappropriate pill splitting by doctors (1%) among 124,300 prescriptions with special oral formulations.

Most respondents didn't receive training in drug stability when splitting OSDFs. A study conducted by Hanssens et al. [51] in Qatar found that the proportion of nurses knowing about OSDFs that should not be crushed after two days' training has increased from 0% to 30%. This indicates without doubt the importance of training for health workers in addition to collaboration between nurses and pharmacists to reduce inappropriate pill splitting and crushing, which would contribute to positive patient

outcomes. This may raise the question about the need of a multidiscipline course with aim to teach and train students in pharmacy, nursing and medicine about common health care practices.

Nearly 66.4% of health workers split tablets, while 39.2% of health workers crushed tablets. More than two-thirds didn’t encourage pill splitting to save money. Similar to what has been found in literature, crushing or splitting OSDFs was a common practice. A study by Nissen et al. [52] found that among nurses who administered medication in a hospital in Australia, 75% crushed tablets.

5. Strengths and limitations of the study

This study is considered the first in Palestine to measure the knowledge, attitudes and practices of health-care practitioners regarding crushing and/or splitting OSDFs.Previous research across the world produced a few studies concerning some parts of this issue.

The participants of this study were selected only from pharmacists and nurses, so one possible limitation was the composition of the participants where medical doctors were not represented as there was a lack of those practitioners in the region. Another limitation of this study is that it was questionnaire based and relied on nurses and pharmacists to determine their actual practice and some answers given may not represent actual practice. The third limitation of the study is that the brief period within which the study was conducted may cause biases for my findings.

6. Conclusions

In conclusion, the study found that nurses' knowledge about splitting or crushing OSDFs was very low compared with that of pharmacists, although this practice is common among nurses. Medical prescriptions including inappropriate tablet splitting or crushing are not rare in clinical practice. This practice may be due to the lack of knowledge of special oral formulations that cannot be split or crushed. The study provided information about special formulations and classes of drugs that must not be split or crushed. Nurses and pharmacists must cooperate with a view to improving pharmaceutical information about these practices. This study raises the requirement of continuing education programs for nurses and pharmacists about this important subject. Moreover, the obtained results, indicate the importance of including a multidisciplinary course for pharmacy, nursing and medical students with the aim of improving their knowledge in many pharmaceutical, clinical and toxicological heath care disciplines in order to minimize potential medication or practice errors during their future carriers.

7. Recommendations

Research in knowledge attitudes is a continual process: it will never end. Therefore the author has some recommendations in order to bring about changes and for future researches in this area

Conducting further observational studies to assess in depth the practice of inappropriate splitting or crushing of OSDFs because they are more accurate than using questionnaires. Also holding regular lectures, educational programs and training for health-care practitioners, especially for nurses to improve their knowledge and practice about splitting or crushing OSDFs and the best ways to do that. Additionally, preparing an information system compiled using up to-date dedicated lists that contain information on crushing, splitting and suspending medicines. I created lists which contained oral solid dosage forms drugs that should not be crushed (Appendix 5). Finally, I suggest a job description for pharmacists through whom they can play a major role in educating nurses about the most important issues when splitting or crushing OSDFs.

References

1. Zaid, A.N., et al., ***Determinants and frequency of pharmaceutical compounding in pharmacy practice in Palestine.*** International Journal of Pharmacy Practice, 2012. **20**(1): p. 9-14.
2. Bachynsky, J., C. Wiens, and k. Melnychuk, **T*he practice of splitting tablets Pharmacoeconomics,*** 2002. **20**(5): p. 339-346.
3. Green, G., et al., *Pharmacopeial standards for the subdivision characteristics of scored tablets.* Pharmacopeial Forum, 2009. **35**: p. 1598-1603.
4. Fawell, N.G., T.L. Cookson, and S.S. Scranton, ***Relationship between tablet splitting and compliance, drug acquisition cost, and patient acceptance.*** American Journal of Health System Pharmacy, 1999. **56**(24): p. 2542-2545.
5. Duncan, M.C., S.S. Castle, and D.S. Streetman, ***Effect of tablet splitting on serum cholesterol concentrations.*** Annual Pharmacotherapy, 2002. **36**(2): p. 205-9.
6. Cohen, J.S., ***Ways to minimize adverse drug reactions. Individualized doses and common sense are key***. Postgrad Medicine, 1999. **106**(3): p. 163-168, 171-172.
7. Van Santen, E., D.M. Barends, and H.W. Frijlink, ***Breaking of scored tablets: a review.*** European Journal of Pharmaceutics and Biopharmaceutics, 2002. **53**(2): p. 139-145.

8. Gill, D., M. Spain, and B. Edlund, ***Crushing or Splitting Medications: Unrecognized Hazards.*** Journal of Gerontological Nursing, 2012. **38**(1): p. 8-12.

9. Root, T., S. Tomlin, and E. D. ***Pharmaceutical Issues when Crushing, Opening or Splitting Oral Dosage Forms*****.** 2011 [cited 2013 23-July]; Available from: http://www.medicinesmanagementstoke.nhs.uk/documents/RPS_Pharmaceutical_Issues_when_Crushing_Opening_Splitting_sdosageforms_june_2011.pdf.

10. Mitchell, J.F. ***Oral dosage forms that should not be crushed***. 2013 [cited 2013 August 18]; Available from: http://www.ismp.org/tools/donotcrush.pdf.

11. Cornish, P., ***"Avoid the crush": hazards of medication administration in patients with dysphagia or a feeding tube***. Canadian Medical Association Journal, 2005. **172**(7): p. 871-872.

12. Shargel, L., A. Yu, and S. Wu-Pongm, ***Applied biopharmaceutics and pharmacokinetics, 6th Edition*****.** 2012, New York: McGraw-Hill.

13. Aulton, M.E., *Pharmaceutics: T***he Design and Manufacture of Medicines.** Fourth Edition ed. 2013, Edinburgh; New York: Churchill Livingstone.

14. Zaid, A.N., ***Attitude and perception of patients and health care practitioners toward oral sustained release dosage forms in Palestine***. Saudi Pharmaceutical Journal, 2010. **18**(4): p. 251-256.

15. Andersen, O., et al., ***[Problems when swallowing tablets. A questionnaire study from general practice]***. Tidsskr Nor Laegeforen, 1995. **115**(8): p. 947-949.

16. Hey, H., et al., ***The passage time for capsules and tablets through the esophagus.*** Ugeskr Laeger, 1983. **145**(32): p. 2432-2435.

17. Overgaard, A.B., et al., ***Patients' evaluation of shape, size and colour of solid dosage forms.*** Pharmcy World and Science, 2001. **23**(5): p. 185-188.

18. Wamberg, T., ***Skal det vaere svaert at sluge tabletter?[Does It Have to Be Difficult Swallowing Tablets?]***. Farmaceutisk Tidende, 1988. **42**: p. 686-690.

19. Karakan, Y., et al., ***A case of ciprofloxacin tablet aspiration.*** Tuberk Toraks, 2010. **58**(1): p. 97-99.

20. Das, N.G. and S.K. Das, ***Controlled release of oral dosage forms.*** Pharmaceutical Technology, 2003. **15**: p. 10-17.

21. De Haan, P. and C.F. Lerk, ***Oral controlled release dosage forms. A review.*** Pharmcy Weekbl Science, 1984. **6**(2): p. 57-67.

22. Pentikis, H., et al., ***Methylphenidate bioavailability in adults when an extended-release multiparticulate formulation is administered sprinkled on food or as an intact capsule.*** Journal of The American Academy of Child and Adolescent Pschiatry, 2002. **41**(4): p. 443-449.

23. Green, G.A., C. Berg, and N. Valdez. ***Lack of Dose Flexibility in Solid Oral Controlled-Release Dosage Forms.***

2009 [cited 2012 July 22]; Available from: http://www.accubreakpharmaceuticals.com/CRS_Abstract_final012909.pdf.

24. Schier, J., et al., ***Fatality from administration of labetalol and crushed extended-release nifedipine.*** **.** The Annals Pharmacotherapy, 2003. **37**(10): p. 1420-1423.
25. Hider, J. and Z. Shehap, ***Effectiveness of modified release isosorbide mononitrate affected by incorrect use,*** in *British Medical Journal* 2000. p. 483.
26. Bowman, C., ***Administration of drugs to patients with swallowing difficulties.*** **J**ournal of the Malta College of Pharmacy Practice, 2007(12): p. 42-45.
27. Mercovich, N., G. Kyle, and M. Naunton, ***Safe to crush? A pilot study into solid dosage form modification in aged care.*** Australasian Journal on Ageing, 2013. **1**: p. 1-5.
28. Akram, G. and A.B. Mullen, ***Paediatric nurses' knowledge and practice of mixing medication into foodstuff.*** The International Journal of Pharmacy Practice, 2012. **20**(3): p. 191-198.
29. Quinzler, R., et al., ***The frequency of inappropriate tablet splitting in primary care.*** European Journal of Clinical Pharmacology, 2006. **62**(12): p. 1065-1073.
30. Rodenhuis, N., P.A.G.M. De Smet, and D.M. Barends, ***The rationale of scored tablets as dosage form.*** European Journal of Pharmaceutical Sciences, 2004. **21**(2): p. 305-308.

31. Lohmann, K., et al., ***Inappropriate crushing information on ward lists: cytotoxic drugs, capsules, and modified release formulations are gravely neglected.*** European Journal of Clinical Pharmacology, 2014. **70**: p. 565-573.

32. Zaid, A.N. and A.A. Ghoush, ***Compliance of Scored Tablet Halves Produced by PalestinianPharmaceutical Companies with the New European PharmacopoeiaRequirements.*** Arch Pharmaceutical Research, 2011. **34**(7): p. 1183-1189.

33. Zaid, A.N., et al., ***Evaluation of the Discrepancy between the European Pharmacopoeia Test and an Adopted United States Pharmacopoeia Test Regarding the Weight Uniformity of Scored Tablet Halves: Is Harmonization Required?*** PDA Journal of Pharmceutical SciencesTechnololgy, 2012. **66**(1): p. 20-27.

34. Freeman, M., W. White, and M. Iranikhah, ***Tablet splitting: a review of weight and content uniformity.*** American Society of Consult Pharmaceutics, 2012. **27**(5): p. 341-352.

35. Noviasky, J., et al., ***Which medications can be split without compromising efficacy and safety?*** Journal of Family Practice, 2006. **55**(8): p. 707-787.

36. Chia-yu, C., et al., ***Association between Physician Specialty and Risk of Prescribing Inappropriate Pill Splitting.*** PloS One, 2013. **8**(7): p. 70-113.

37. Quinzler, R., J. Szecsenyi, and W.E. Haefeli, ***Tablet splitting: patients and physicians need better support.*** European Journal of Clininical Pharmacology, 2007. **63**(12): p. 1203-1204.

38. Ministry of Health and PHIC. ***Health Report Mid Year 2013.*** 2013 [cited 2014 September 16]; Available from: http://www.moh.ps/attach/546.pdf.

39. Khdour, M.R. and H.O. Hallak ***Societal perspectives on community pharmacy services in West Bank-Palestine.*** Pharmacy Practice, 2012. **10**(1): p. 17-24.

40. Sawalha, A.F., ***Consumption of Prescription and non-Prescription Medications by Pregnant Women.*** The Islamic University Journal, 2007. **2**(15): p. 41-57.

41. Jaradat, N. and W. Sweileh, ***A Descriptive Study of Community Pharmacy Practice in Palestine: Analysis and Future Look.*** An-Najah University Journal for Research, 2003. **17**(2): p. 287-300.

42. Giacaman, R., H.F. Abdul-Rahim, and L. Wick, ***Sector reform in the Occupied Palestinian Territories (OPT): targeting the forest or the trees? Health policy plan*** **Oxford Journals, 2003. 18**(1): p. 59-67.

43. Obeidallah, W., et al., ***Drug situation analysis for the West Bank and Gaza Strip. WHO,.*** **2000,** Switzerland: World Health Organisation: .

44. Palestinian Central Bureau of Statistics**.** ***Palestine in Figures 2013.*** 2014 [cited 2014 September 16]; Available from:

http://www.pcbs.gov.ps/Portals/_PCBS/Downloads/book2040.pdf.

45. Mafiana, R.N., A. Tagi, and I. Al-Zakwani, ***Evaluation of nurses' knowledge of oral solid dosage forms that should not be crushed at a university hospital in Oman.*** Royal Pharmaceutical Society, 2013. **5**: p. 49-53.

46. Dashti-Khavidaki, S., et al., ***The role of clinical pharmacist to improve medication administration through enteral feeding tubes by nurses***. International Journal of Clinical Pharmacy, 2012. **34**(5): p. 757-764.

47. Green, C.F., et al., ***Attitudes and knowledge of hospital pharmacists to adverse drug reaction reporting.*** British Journal of Clinical Pharmacology, 2008. **51**(1): p. 81-86.

48. Hanafi, S., et al., ***Knowledge, attitudes and practice of nurse regarding adverse drug reaction reporting.*** Iran Journal of Nurse Midwifery Research, 2012. **17**(1): p. 21-25.

49. Ahmad, A., et al., ***An evaluation of knowledge, attitude and practice of Indian pharmacists towards adverse drug reaction reporting: A pilot study.*** Perspect of Clinical Research, 2013. **4**(4): p. 204-210.

50. Al-Ramahi, R., et al., ***Attitudes of consumers and healthcare professionals towards the patient package inserts - a study in Palestine.*** Pharmacy Practice, 2012. **10**(1): p. 57-63.

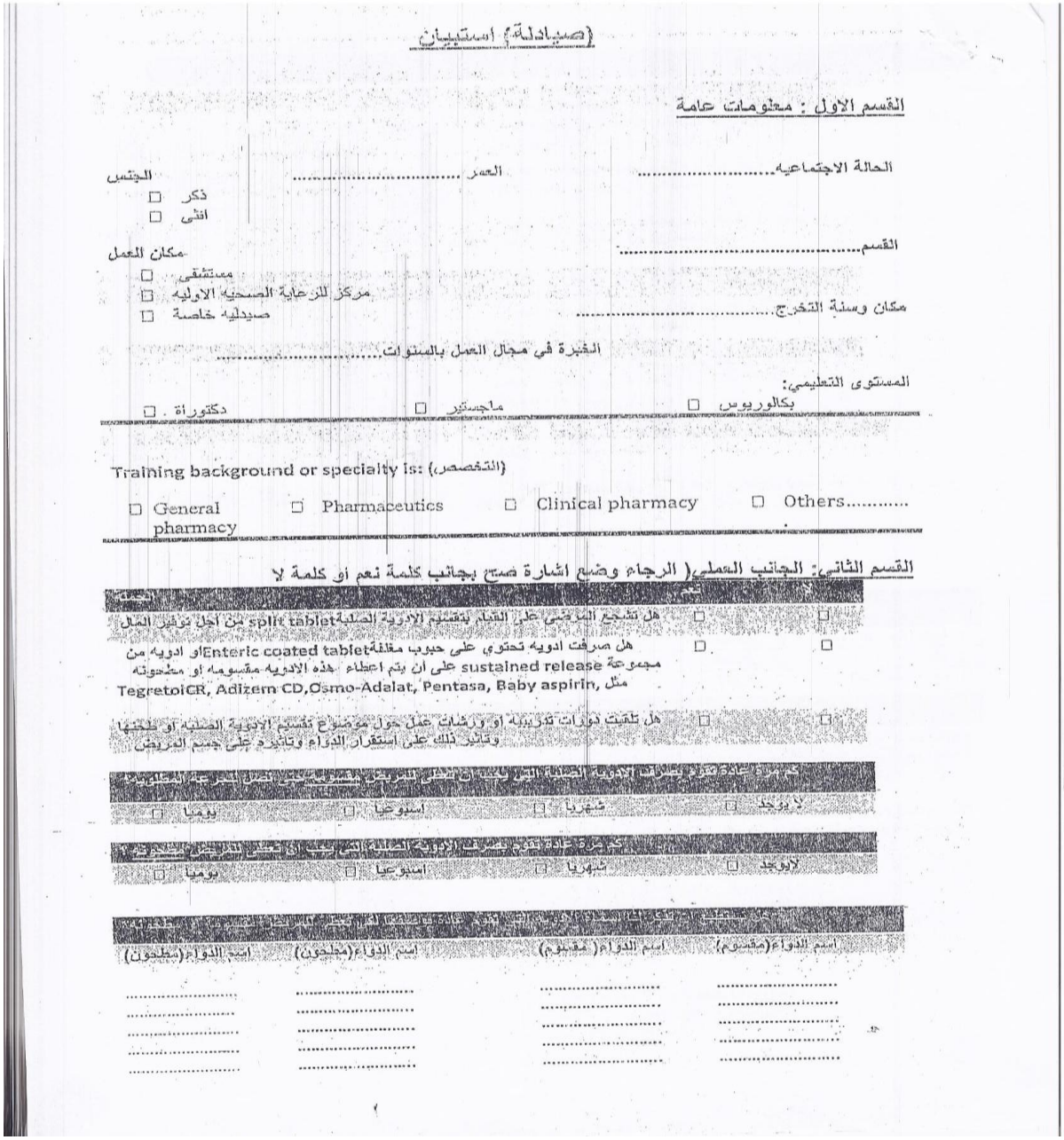
51. Hanssens, Y., et al., ***Improving oral medicine administration in patients with swallowing problems and feeding tubes.*** Annal Pharmacotherapy., 2006. **40**(12): p. 2142-2147.

52. Nissen, L., A. Haywood, and K. Steadman, ***Solid Medication Dosage Form Modification at the Bedside and in the Pharmacy of Queensland Hospitals.*** Journal of Pharmacy Practice and Research, 2009. **39**(2): p. 129-134.

Appendices

Appendix (1)

Questionnaire for pharmacists



(صيادلة) استبيان

القسم الاول : معلومات عامة

الحالة الاجتماعيه..... العمر ..... الجنس

☐ ذكر
☐ انثى

القسم.....

مكان العمل

☐ مستشفى
☐ مركز للرعاية الصحيه الاوليه
☐ صيدليه خاصة

مكان وسنة التخرج.....

الخبرة في مجال العمل بالسنوات.....

المستوى التعليمي:

☐ بكالوريوس ☐ ماجستير ☐ دكتوراة .

Training background or specialty is: (التخصص)

☐ General pharmacy ☐ Pharmaceutics ☐ Clinical pharmacy ☐ Others.....

القسم الثاني: الجانب العملي (الرجاء وضع اشارة صح بجانب كلمة نعم او كلمة لا

	نعم	لا
هل تشجع المرضى على القيام بتقسيم الادوية الصلبة split tablet من اجل توفير المال	☐	☐
هل صرفت ادويه تحتوي على حبوب مغلفة Enteric coated tablet او ادويه من مجموعة sustained release على ان يتم اعطاء هذه الادويه مقسومه او مطحونه مثل TegretolCR, Adizem CD,Osmo-Adalat, Pentasa, Baby aspirin,	☐	☐
هل تلقيت دورات تدريبية او ورشات عمل حول موضوع تقسيم الادوية الصلبه او طحنها وتاثير ذلك على استقرار الدواء وتاثيره على جسم المريض	☐	☐

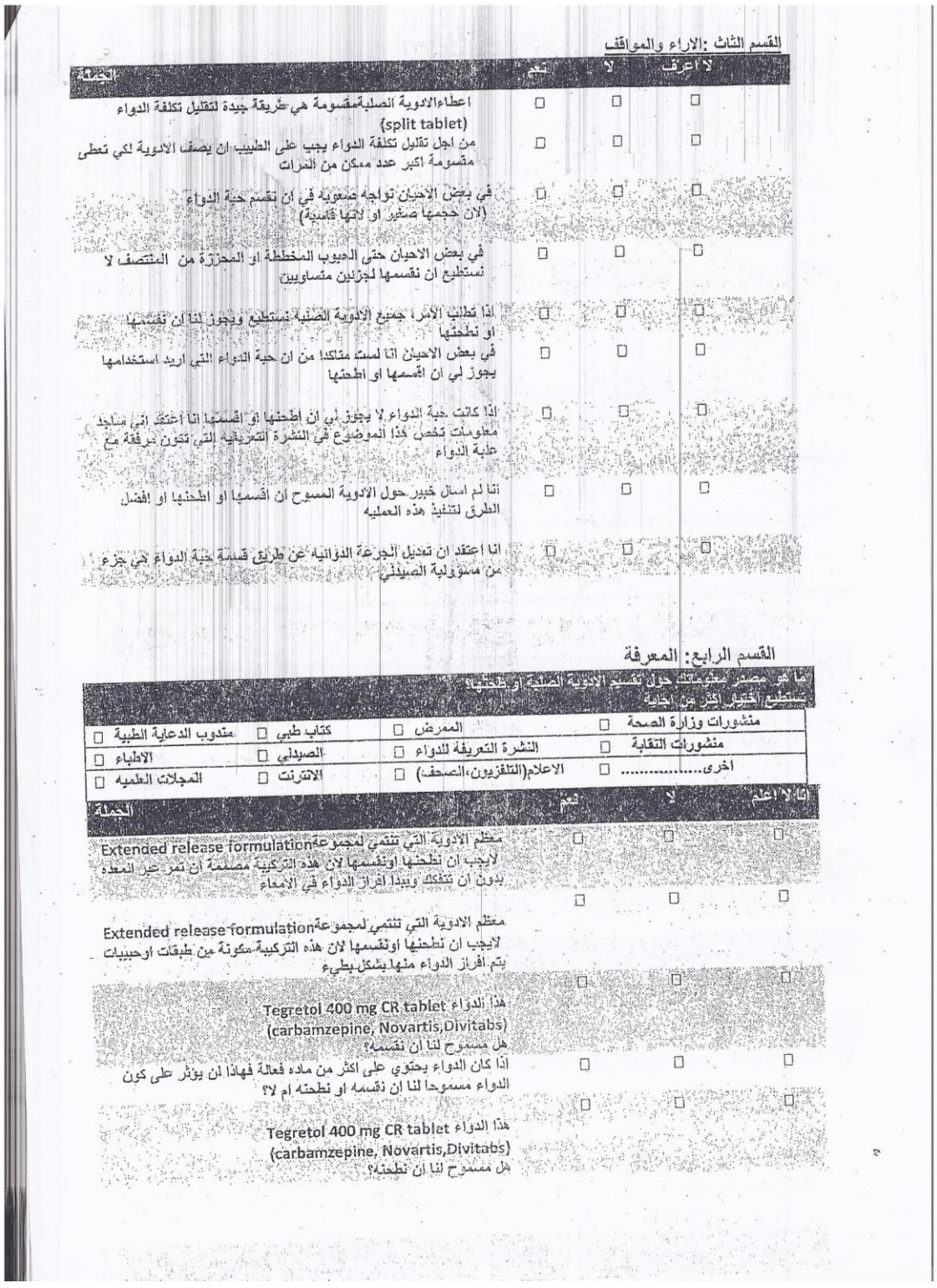
كم مرة تقوم بصرف الادوية التي تحتاج الى تقسيم او طحن

☐ يوميا ☐ اسبوعيا ☐ شهريا ☐ لا يوجد

كم مرة تقوم بصرف الادوية التي تحتاج الى تقسيم او طحن

☐ يوميا ☐ اسبوعيا ☐ شهريا ☐ لا يوجد

اسم الدواء (مقسوم)	اسم الدواء (مقسوم)	اسم الدواء (مطحون)	اسم الدواء (مطحون)
.....	.....	.....	.....
.....	.....	.....	.....
.....	.....	.....	.....
.....	.....	.....	.....
.....	.....	.....	.....



القسم الثالث :الاراء والمواقف

الجملة	نعم	لا	لا اعرف
اعطاءالادوية الصلبةمقسومة هي طريقة جيدة لتقليل تكلفة الدواء (split tablet)	☐	☐	☐
من اجل تقليل تكلفة الدواء يجب على الطبيب ان يصف الادوية لكي تعطى مقسومة اكبر عدد ممكن من المرات	☐	☐	☐
في بعض الاحيان تواجه صعوبة في ان تقسم حبة الدواء (لان حجمها صغير او لانها قاسية)	☐	☐	☐
في بعض الاحيان حتى الدبوب المخططة او المحززة من المنتصف لا نستطيع ان نقسمها لجزئين متساويين	☐	☐	☐
اذا تطلب الامر، جميع الادوية الصلبة نستطيع ويجوز لنا ان نقسمها او نطحنها	☐	☐	☐
في بعض الاحيان انا لست متاكدا من ان حبة الدواء التي اريد استخدامها يجوز لي ان اقسمها او اطحنها	☐	☐	☐
اذا كانت حبة الدواء لا يجوز لي ان اطحنها او اقسمها انا اعتقد انني سأجد معلومات تخص هذا الموضوع في النشرة التعريفية التي تكون مرفقة مع علبة الدواء	☐	☐	☐
انا لم اسال خبير حول الادوية المسموح ان اقسمها او اطحنها او افضل الطرق لتنفيذ هذه العمليه	☐	☐	☐
انا اعتقد ان تعديل الجرعة الدوائيه عن طريق قسمة حبة الدواء هي جزء من مسئولية الصيدلي	☐	☐	☐

القسم الرابع: المعرفة

ما هو مصدر معلوماتك حول تقسيم الادوية الصلبة او طحنها؟
يستطيع اختيار اكثر من اجابة

منشورات وزارة الصحة ☐	المعرض ☐	كتاب طبي ☐	مندوب الدعاية الطبية ☐
منشورات النقابة ☐	النشرة التعريفة للدواء ☐	الصيدلي ☐	الاطباء ☐
اخرى..... ☐	الاعلام(التلفزيون،الصحف) ☐	الانترنت ☐	المجلات العلميه ☐

الجملة	نعم	لا	لا اعلم
معظم الادوية التي تنتمي لمجموعةExtended release formulation لايجب ان نطحنها اونقسمها لان هذه التركيبة مصممة ان تمر عبر المعده بدون ان تتفكك ويبدا افراز الدواء في الامعاء	☐	☐	☐
معظم الادوية التي تنتمي لمجموعةExtended release formulation لايجب ان نطحنها اونقسمها لان هذه التركيبة مكونة من طبقات اوحبيبات يتم افراز الدواء منها بشكل بطيء	☐	☐	☐
هذا الدواء Tegretol 400 mg CR tablet (carbamzepine, Novartis,Divitabs) هل مسموح لنا ان نقسمه؟	☐	☐	☐
اذا كان الدواء يحتوي على اكثر من ماده فعالة فهاذا لن يؤثر على كون الدواء مسموحا لنا ان نقسمه او نطحنه ام لا؟	☐	☐	☐
هذا الدواء Tegretol 400 mg CR tablet (carbamzepine, Novartis,Divitabs) هل مسموح لنا ان نطحنه؟	☐	☐	☐

الجملة	Enteric coated	Extended release	لا اعلم
هذا الدواء Baby Aspirin cardio (acetyl salicylic acid, Bayer company) لا يجب ان نطحنه او نقسمه لانه:	☐	☐	☐
هذا الدواء (للدهنيات) Lescol XL (fluvastatin, Novartis company) لا يجب ان نطحنه او نقسمه لانه:	☐	☐	☐

ITEM	يزيد من تركيز الدواء وبالتالي زيادةtoxicity السميه	يبطل مفعول المادة الفعالة Inactivate	لااعرف
هذا الدواء Omeprazole(للقرحة) enteric coated granule لا يجب ان نطحنة او نقسمه لان ذلك:	☐	☐	☐
اعطاء هذا الدواء مطحونNifedipineXLtablet سوف يؤدي الى:	☐	☐	☐
هذا الدواءPancreatinدواء يشبه انزيمات البنكرياس لا يجب ان نطحنه او نقسمه لان ذلك:	☐	☐	☐

حبوب الادويه المضاده للسرطانAntineoplastic agent لا يجب ان تقسيما او تطحنها لان ذلك:

انا لا اعرف ☐ | يعرض الذين يتعاملون معها لمخاطر صحيه ☐ | يبطل مفعول المادة الفعالة Inactivate ☐

هذا الدواءالذي يستخدم لعلاج الضغط وامراض القلب يجب ان لا تطحنه لماذا؟ Nefidipne coated tablet

انا لا اعرف ☐ | يزيد من تركيز الدواء وبالتالي زيادةtoxicity السميه ☐ | هذا الدواء حساس جدا للضوء ☐

ان اعطاء دواء enteric coated sulphasalazine(دواء يعطى لعلاج التهاب المفاصل)مطحون او مفتوح يؤدي الى:

انا لا اعرف ☐ | The drug being released too early خروج المادة الفعالة قبل وصولها المكان المستهدف ☐ | يزيد من تركيز الدواء وبالتالي زيادةtoxicity السميه ☐

حبوب Alendronate(دواء يستخدم لعلاج هشاشة العظام)يجب جلوس المريض بعد تناولها قبل شربه بسبب:

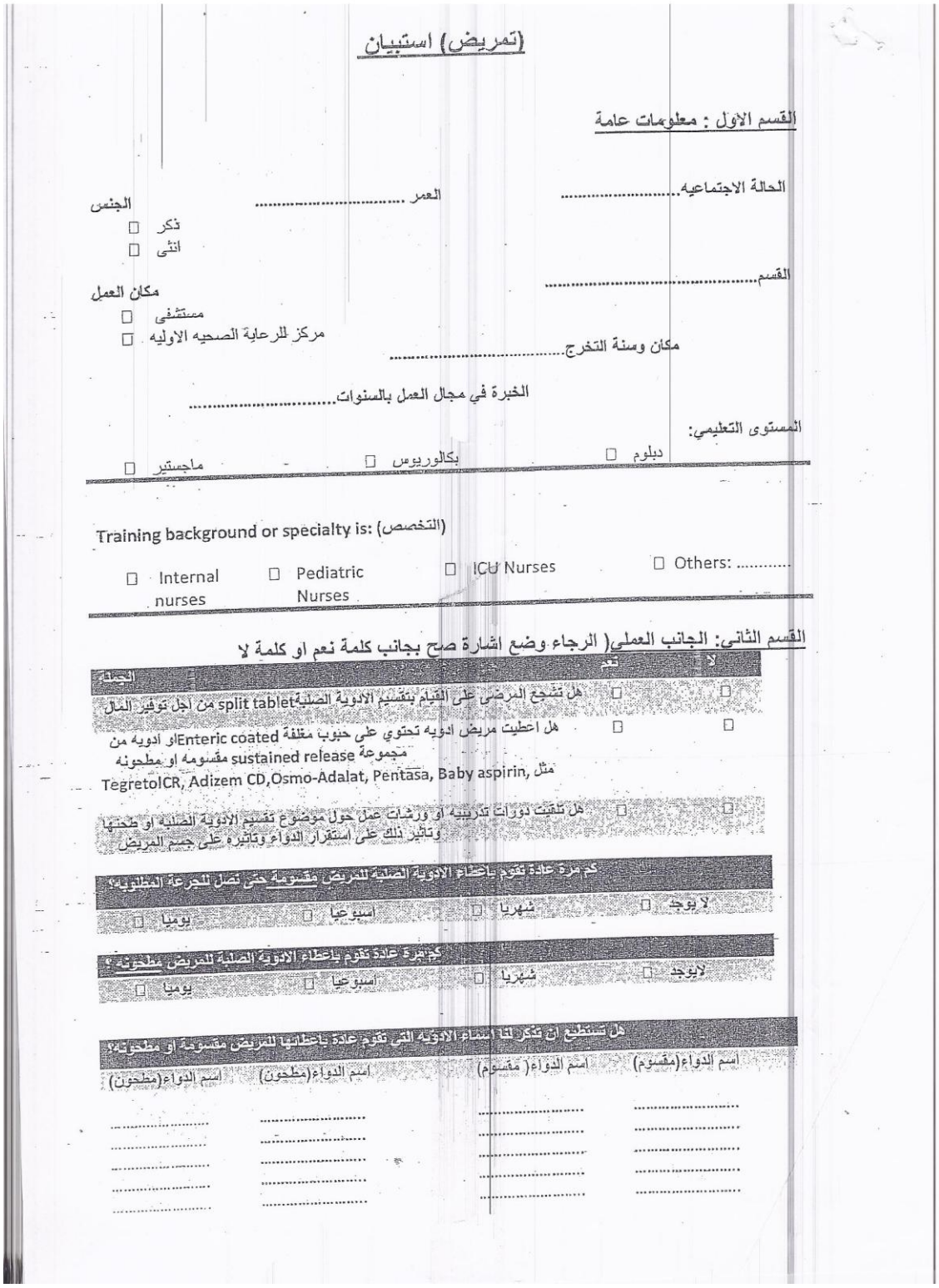
انا لا اعرف ☐ | انه يؤدي الى اعراض جانبيه esophageal irritation ☐ | انه يبطل مفعول المادة الفعالة Inactivate ☐

شكرا جزيلا على تعاونك

انتهى الاستبيان

Appendix (2)

Questionnaire for nurses



(تمريض) استبيان

القسم الاول : معلومات عامة

الحالة الاجتماعيه.....

العمر .....

الجنس
ذكر ☐
انثى ☐

القسم.....

مكان العمل
مستشفى ☐
مركز للرعاية الصحيه الاوليه ☐

مكان وسنة التخرج.....

الخبرة في مجال العمل بالسنوات.....

المستوى التعليمي:
دبلوم ☐ بكالوريوس ☐ ماجستير ☐

Training background or specialty is: (التخصص)

☐ Internal nurses ☐ Pediatric Nurses ☐ ICU Nurses ☐ Others: .....

القسم الثاني: الجانب العملي(الرجاء وضع اشارة صح بجانب كلمة نعم او كلمة لا

الجمله	نعم	لا
هل تنصح المرضى على القيام بتقسيم الادوية الصلبةsplit tablet من اجل توفير المال	☐	☐
هل اعطيت مريض ادويه تحتوي على حبوب مغلفة Enteric coated او ادويه من مجموعة sustained release مقسومه او مطحونه مثل TegretolCR, Adizem CD,Osmo-Adalat, Pentasa, Baby aspirin,	☐	☐
هل تلقيت دورات تدريبيه او ورشات عمل حول موضوع تقسيم الادوية الصلبه او طحنها وتاثير ذلك على استقرار الدواء وتاثيره على جسم المريض	☐	☐

كم مرة عادة تقوم باعطاء الادوية الصلبة للمريض مقسومة حتى تصل للجرعة المطلوبة؟

لا يوجد ☐ شهريا ☐ اسبوعيا ☐ يوميا ☐

كم مرة عادة تقوم باعطاء الادوية الصلبة للمريض مطحونة ؟

لا يوجد ☐ شهريا ☐ اسبوعيا ☐ يوميا ☐

هل تستطيع ان تذكر لنا اسماء الادوية التي تقوم عادة باعطائها للمريض مقسومة او مطحونة؟

اسم الدواء(مقسوم)	اسم الدواء(مقسوم)	اسم الدواء(مطحون)	اسم الدواء(مطحون)
.....	.....	.....	.....
.....	.....	.....	.....
.....	.....	.....	.....
.....	.....	.....	.....
.....	.....	.....	.....

القسم الثالث :الاراء والمواقف

الجملة	نعم	لا	لا أعرف
اعطاءالادوية الصلبةمقسومة هي طريقة جيدة لتقليل تكلفة الدواء (split tablet)	☐	☐	☐
من اجل تقليل تكلفة الدواء يجب على الطبيب ان يصف الادوية لكي تعطى مقسومة اكبر عدد ممكن من المرات	☐	☐	☐
في بعض الاحيان نواجه صعوبه في ان نقسم حبة الدواء (لان حجمها صغير او لانها قاسية)	☐	☐	☐
في بعض الاحيان حتى الحبوب المخططة او المحززة من المنتصف لا نستطيع ان نقسمها لجزئين متساويين	☐	☐	☐
اذا تطلب الامر، جميع الادوية الصلبة نستطيع ويجوز لنا ان نقسمها او نطحنها	☐	☐	☐
في بعض الاحيان انا لست متاكدا من ان حبة الدواء التي اريد استخدامها يجوز لي ان اقسمها او اطحنها	☐	☐	☐
اذا كانت حبة الدواء لا يجوز لي ان اطحنها او اقسمها انا اعتقد انني سأجد معلومات تخص هذا الموضوع في النشرة التعريفيه التي تكون مرفقة مع علبة الدواء	☐	☐	☐
انا لم اسال خبير حول الادوية المسموح ان اقسمها او اطحنها او افضل الطرق لتنفيذ هذه العمليه	☐	☐	☐
انا اعتقد ان تعديل الجرعة الدوائيه عن طريق قسمة حبة الدواء هي جزء من مسؤولية الممرض	☐	☐	☐

القسم الرابع: المعرفة

ما هي مصادر معلوماتك حول تقسيم الادوية الصلبة او طحنها؟
يستطيع اختيار اكثر من اجابة

منشورات وزارة الصحة ☐	الممرض ☐	كتاب طبي ☐	مندوب الدعاية الطبية ☐
منشورات النقابة ☐	النشرة التعريفة للدواء ☐	الصيدلي ☐	الاطباء ☐
اخرى..... ☐	الاعلام(التلفزيون،الصحف) ☐	الانترنت ☐	المجلات العلميه ☐

الجملة	نعم	لا	انا لا اعلم
معظم الادوية التي تنتمي لمجموعةExtended release formulation لايجب ان نطحنها اونقسمها لان هذه التركيبة مصممة ان تمر عبر المعدة بدون ان تتفكك ويبدا افراز الدواء في الامعاء	☐	☐	☐
معظم الادوية التي تنتمي لمجموعةExtended release formulation لايجب ان نطحنها اونقسمها لان هذه التركيبة مكونة من طبقات اوحبيبات يتم افراز الدواء منها بشكل بطيء	☐	☐	☐
هذا الدواء Tegretol 400 mg CR tablet (carbamzepine, Novartis,Divitabs) هل مسموح لنا ان نقسمه؟	☐	☐	☐
اذا كان الدواء يحتوي على اكثر من ماده فعالة فهاذا لن يؤثر على كون الدواء مسموحا لنا ان نقسمه او نطحنه ام لا؟	☐	☐	☐
هذا الدواء Tegretol 400 mg CR tablet (carbamzepine, Novartis,Divitabs) هل مسموح لنا ان نطحنه؟	☐	☐	☐

الجملة	Enteric coated	Extended release	لا اعلم
هذا الدواء Baby Aspirin cardio (acetyl salicylic acid, Bayer company لا يجب ان نطحنه او نقسمه لانه:	☐	☐	☐
هذا الدواء (للدهنيات) Lescol XL (fluvastatin, Novartis company) لا يجب ان نطحنه او نقسمه لانه:	☐	☐	☐

ITEM	يزيد من تركيز الدواء وبالتالي زيادة السميه toxicity	يبطل مفعول المادة الفعالة Inactivate	لااعرف
هذا الدواء Omeprazole(للقرحة) enteric coated granule لا يجب ان نطحنه او نقسمه لان ذلك:	☐	☐	☐
اعطاء هذا الدواء مطحون NifedipineXLtablet سوف يؤدي الى:	☐	☐	☐
هذا الدواء Pancreatin دواء يشبه انزيمات البنكرياس لا يجب ان نطحنه او نقسمه لان ذلك:	☐	☐	☐

حبوب الادويه المضاده للسرطان Antineoplastic agent لا يجب ان نقسمها او نطحنها لان ذلك:

انا لا اعرف ☐ يعرض الذين يتعاملون معها لمخاطر صحيه ☐ يبطل مفعول المادة الفعالة Inactivate ☐

Nefidipne coated tablet هذا الدواء الذي يستخدم لعلاج الضغط وامراض القلب يجب ان لا نطحنه لماذا؟

انا لا اعرف ☐ يزيد من تركيز الدواء وبالتالي زيادة السميه toxicity ☐ هذا الدواء حساس جدا للضوء ☐

ان اعطاء دواء enteric coated sulphasalazine (دواء يستخدم لعلاج التهاب القولون) مطحون او مقسم يؤدي الى:

انا لا اعرف ☐ The drug being released too early خروج المادة الفعالة قبل وصولها المكان المستهدف ☐ يزيد من تركيز الدواء وبالتالي زيادة السميه toxicity ☐

حبوب Alendronate (دواء يستخدم لعلاج هشاشة العظام) يجب عدم طحنه لانه سوف يسبب:

انا لا اعرف ☐ انه يؤدي الى اعراض جانبيه esophageal irritation ☐ انه يبطل مفعول المادة الفعالة Inactivate ☐

شكرا جزيلا على تعاونك

انتهى الاستبيان

Appendix (3)

IRB Approval

An-Najah
National University
Faculty of Medicine

بسم الله الرحمن الرحيم

جامعة
النجاح الوطنية
كلية الطب

IRB Approval letter

Study title:
Attitudes, knowledge and perception of health care practitioners toward splitting or crushing oral solid dosage form in Palestine: Safety and therapeutic implication.

Submitted by:
Yaser Mustafa Mahmoud Abdallah

Date Reviewed:
July 12, 2012

Date approved:
August 6, 2012

Your study titled " **Attitudes, knowledge and perception of health care practitioners toward splitting or crushing oral solid dosage form in Palestine: Safety and therapeutic implication** " Was reviewed by An-Najah National University IRB committee & approved on August 6, 2012

Samar Musmar,MD, FAAFP
IRB Committee Chairman,
An-Najah National University

IRB

نابلس - ص.ب ٧٠٧,٧ هاتف: ١٤/٨/٧/٤/٢ ٠٢٣٤٢٩٠٢(٠٩)(٩٧٢)، فاكسميل ٢٣٤٩٧٣٩(٠٩)(٩٧٢)
Nablus - P.O.Box 7,707 - Tel. (972)(09)2342902/4/7/8/14 - Facximile (972)(09)2349739
Web Site:www.najah.edu

Appendix (4)

Palestinian Ministry of Health Approval

30 Nov 2014 7:12 HP Fax page 1

Palestinian National Authority
Ministry of Health - Nablus
General Directorate of Higher & Continuning Education

السلطة الوطنية الفلسطينية
وزارة الصحة- نابلس
الإدارة العامة للتعليم الصحي

Ref.: .....
Date:.....

الرقم: ٢٠١٤/٣٠٣/١٦٢ ق
التاريخ: ٢٠١٤/١٢/٣٠ ق

الأخ ق. أ. مدير عام الإدارة العامة للمستشفيات المحترم،،،
الأخ مدير مجمع فلسطين الطبي المحترم،،،
تحية واحترام،،

الموضوع: تسهيل مهمة طلاب – جامعة النجاح

تماشياً مع سياسة وزارة الصحة المتعلقة بتعزيز التعاون مع الجامعات والمؤسسات الأكاديمية بإتاحة فرص التدريب أمام الطلبة والخريجين والباحثين في المؤسسات الوطنية وإسهاماً في تنمية قدراتهم.

يرجى تسهيل مهمة الطالب ياسر مصطفى محمود عبد الله– ماجستير برنامج الصيدلة السريرية كلية الطب وعلوم الصحة/ جامعة النجاح في اجراء بحث بعنوان "تقييم مدى المعرفة والممارسة في كسر او طحن الأدوية الصلبة في فلسطين ودراستها من الناحية العلاجية والسمية "، وذلك من خلال السماح للطالب بمقابلة بعض الأطباء والصيادلة والممرضين والاستفسار عن بعض المعلومات التي يحتاجها الطالب لانجاز البحث، وذلك في كافة المستشفيات، مع العلم أن الطالب سيلتزم بمعايير البحث العلمي ويلتزم بالحفاظ على سرية المعلومات.

– مع ضرورة موافاتنا بنسخة من نتائج البحث.

مع التقدير،،

د. أمل أبو عوض
ق. أ. مدير عام التعليم الصحي

/ نسخة مدير دائرة الصيدلة المحترم –جامعة النجاح

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تلفون: 09-2384771-6 فاكس: 09-2384777

Appendix (5)

Oral Solid Dosage Forms That Should Not Be Crushed

Drug Product	Active ingredient(s)	Dosage forms	Reasons /Comments
-	Rabeprazole	Tablet	Extended- release
-	Fentany	Lozenge	Slow-release
Actonel	Risedronate	Tablet	Irritant Note: chewed crushed or sucked tablets cause oropharyngeal irritation
Osmo-Adalat	Nifedipine	Tablet	Slow-release
-	Amphetamine salts	Capsule	Extended- release
Afinitor	Everolimus	Tablet	Mucus membrane irritant
Aggrenox	Combination	Capsule	Extended- release
Allegra-D	Combination	Tablet	Extended- release
-	Alprazolam	Tablet	Extended- release
-	Lovastatin	Tablet	Extended- release
-	zolpidem	Tablet	Extended- release
Wellbutrin XR Zyban SR	Bupropion	Tablet	Extended- release

Drug Product	Active ingredient(s)	Dosage forms	Reasons /Comments
Pentasa SR Granule	Mezalamine	Granule	Slow- release Maintain PH at less than or equal 6
Pentasa	Mezalamne	Capsule	Slow release (a)
Aricept 23 mg	Donepezil	Tablet	Note: crushing 23mg tablet may cause significantly increase the rate of absorption , but the 5,10mg are not affected.
Arthrotec	Combination	Tablet	Delay release, Enteric coated.
Asacol	Mesalamine	Tablet	Slow- release
Aspirin cardio, Tevapirin Cartia	Aspirin	Tablet	Enteric coated
Rafassal prolnged release Granules	Mesalamine	Granules	Extended- release
Raffasal	5- aminosalicylic acid	Caplet	Enteric coated

Drug Product	Active ingredient(s)	Dosage forms	Reasons /Comments
Avodart	dutasteride	Capsule	Note: Drug may cause fatal abnormalities; women who are, or become pregnant, should not handle capsule, all women should use caution in handling capsule, especially leaking capsule,
Duodart		Capsule	Note: Drug may cause fatal abnormalities; women who are, or become pregnant, should not handle capsule, all women should use caution in handling capsule, especially leaking capsule,
KLACID XL KLARICAREXL	Clarithromycin	Tablet	Extended- release
VerapressSR	Verapamil	Caplet	Extended-release
Tegretol CR Teril CR	Carbamazepine	Tablet	Extended-release
Slow-Deralin	Propranolol	Tablet	Slow- release
Cardizem LA	Diltiazem	Tablet	Extended-release
Cefaclor ER	Combination	Tablet	Extended-release
Zinnat Zinaxim	Cefuroxime	Tablet	Taste Note:use suspension for children
Cellcept MYCOPHENOLATE	Mycophenolate	Capsule, Tablet	Teratogenic potensial
Ciprocare XR	Ciproflxacin	Tablet	Extended-release
Klaricare XL Klacid XL	Klarithromycin	Tablet	Extended-release
Concerta Ritalin SR	Methyphenidate	Tablet	Extended-release
Etopan XL Etodolac ER	Etodolac	Tablet	Extended-release
Theotard	Theophyllin	Capsule	Slow- release (a)
Creon	Pancrelipase	Capsule	Extended-release (a)

Drug Product	Active ingredient(s)	Dosage forms	Reasons /Comments
Crixivan	Indinavir	Capsule	Taste Note: capsule may be opened and mixed with fruit puree (e,g., banana)
Cymbelta	Duloxetine	Capsule	Extended-release (a) Note: may add contents of capsule to apple juice or apple applesauce but not chocolate
Valcyte	Ganciclovir	Tablet	Skin irritant
Detrusitol SR	Tolterodine L-Tartarate	Capsule	Extended-release
Crixivan	Indinavir	Capsule	Taste Note: capsule may be opened and mixed with fruit puree (e,g., banana)
Cymbelta	Duloxetine	Capsule	Extended-release (a) Note: may add contents of capsule to apple juice or apple applesauce but not chocolate
Valcyte	Ganciclovir	Tablet	Skin irritant
Detrusitol SR	Tolterodine L-Tartarate	Capsule	Extended-release
Depalept	Sodium Valproate	Tablet	Enteric coated
Depalept Chrono	Sodium valproate and Valproic acid	Tablet	Extended-release
Abitrin Sustained Dclofen SR Voltaren Retard Rufenal SR Betaren SR	Diclofenac Sodium	Tablet	Extended-release
Ferrograd folic Slow- Fe- Folic	Combination	Tablet	Extended-release
Advil Ultrafen LC Nurofen Forte	Ibubrufen	LiquiCap	Liquid filled (d)
Droxia	Hudroxy urea	Capsule	Note: exposure to the powder may cause serious skin toxicities, healthcare workers should wear gloves to administer.

Drug Product	Active ingredient(s)	Dosage forms	Reasons /Comments
Cal-c-via (Bayer) Zimcal	Multivitamin and Multimineral	Effervescent Tablet	Effervescent Tablet (f)
Calcium + Vitamin D3 (Sun life) Magnesium +B complex (spectru vit) Calcium + Vitamin D3 (spectru vit)	Multivitamin and Multimineral	Effervescent Tablet	Effervescent Tablet (f)
Orset Zinc + Iron+folic acid (Sun life)	Multimineral	Effervescent Tablet	Effervescent Tablet (f)
Multi Vitamins (spectru vit) Vitamin C (spectru vit)	Multivitamin	Effervescent Tablet	Effervescent Tablet (f)
Dialatam SR	Diltiazem	Tablet	Extended-release
Topamax	Topiraamte	Tablet, Capsule	Taste, Taste(a)
Trental	Pentoxifylin	Tablet	Extended-release
Anafranil SR	Clomipramin	Tablet	Extended-release
Effexor XR	Venalfaxin	Capsule	Extended-release
Evista	raloxifene	Tablet	Taste, Teratogenic potential (i)

Drug Product	Active ingredient(s)	Dosage forms	Reasons /Comments
Exjade	Deferasirox	Tablet	Note: do not give as tablet , Tablets are meant to be given as a liquid, see company insert
Tamsulosin-Teva Omnic OCAS	Tamsulosin	Capsule	Extended-release
Gripmin SR	Combination	Capsule	Extended-release
Decongex SR	Combination	Tablet	Extended-release
Swiss Relief	Diclofenac sodium	Capsule	Extended-release
Pantover Contraloc	Pantoprazole	Tablet	Enteric-coated
Flagyl ER	Metronidazole	Tablet	Extended-release
Osteotab Fosmax Alendronate- Teva Bonadex	Alendrnate	Tablet	Mucous membrane irritant

Drug Product	Active ingredient(s)	Dosage forms	Reasons /Comments
Glucophage XR	Metformin	Tablet	Extended-release
Gleevac	Imatinib	Tablet	Taste (h) Note: may be dissolved in water or apple jauice
Janumet XR	Combination	Tablet	Extended-release
Isosupra Lidose Roaccutane Curatane	Isotretinion	Tablet	Mucus membrane irritant
Cordil SR Isoket Retard	Isoorbide Dinitrate	Tablet	Extended-release
Nitrostat Sublingaul	Nitroglycerin (sublingual)	Tablet (sublingual)	(g)
Cordil sublingual Isoket sublingual	Isosorbide Dinitrate	Tablet (sublingual)	(g)
Keppra XR	Levetiracetam	Tablet	Extended-release (b)
Tamoxfen- Teva	Tamoxifen	Tablet	Exposure to the powder may cause carcinogenic and teratogenic potential, women who are, or become pregnant, should not handle capsule, all women should use caution in handling tablet

Drug Product	Active ingredient(s)	Dosage forms	Reasons /Comments
Xanagis XR	Alprazolam	Tablet	Extended-release
Nexiumc	Esomeprzole	Tablet, Capsule	Gastro resistant tablet, Delay release (a)
Omeprdex Mepral Marial Omeprazole-Teva Omepra Losec Locid	Omeprazole	Capsule	Granules inside capsule If necessary, the capsule may be opened its content mixed with soft acidic food or an acidic beverage (such as orange jauice) and swallowed immediately

Drug Product	Active ingredient(s)	Dosage forms	Reasons /Comments
Lanton Lansoprazole - Teva	Lansoprazole	Capsule	Granules inside capsule If necessary, the capsule may be opened and the granules inside it placed on the tongue to be swallowed immediately or its content mixed with soft acidic food or an acidic beverage (such as orange jauice) and swallowed immediately
Seroquel XR	Quetiapine	Tablet	Extended-release
Ritalin LA	Methylphenidate	Capsule	Extended-release
Requip XL	Ropinirole	Tablet	Extended-release
Rapamune	Sirolimus	Tablet	Note:pharmacokinetic nanocrstal technology may be affected (b)
Verapress DR	Verapamil	Caplet	Extended-release
-	Linalidomide	Capsule	Note:teratogenic potential, healthworkers should avoid contact capsule contact body fluid.

Drug Product	Active ingredient(s)	Dosage forms	Reasons /Comments
Procure Propecia Finacia	Finasteride	Tablet	Women who are ,or become pregnant should not handle broken or crushed tablets.
Prozac Weekly	Fluoxetine	Tablet	Enteric coated
-	Ritonavir	Tablet	Note: crushing tablets has resulted in decreased bioavailability of drug (b)
-	Oxycocdon	Tablet	Extended-release Note: tablet disruption may cause a potential fatal overdose of oxycododne
-	Tapentadone	Tablet	Extended-release Note: toxic dose may occur if tablet is split or crushed, causing rapid release and absorbtion of potential fatal dose.
	dapigatrin	Capsule	Note: bioavailability increases by 75% when the pellets are taken without the capsule shell
Tramal Long	Tramadol	Tablet	Extended-release Note: crushing may cause overdose
Tasigna	Nilotinib	Capsule	Note: disruption of capsule may yield high blood level causing enhanced toxicity
Temodal	Temozolomid	Capsule	Note: accidentally opened or damaged capsules require rigorous precautions to avoid inhalation or contact with the skin or mucous membranes
Valcyte	Valganciclovir	Tablet	Teratogenic and irritant potential (i,b)
-	Budisonide	Tablet	Note: coating on tablet

			is designed to breake down at PH of 7.0 or above
Tovias	Fesoteridne	Tablet	Extended-release
Votrient	Pazopanib	Tablet	Note: crushing significantly increases the AUC and T max, crushed or broken tablets may cause dangerous skin problems
Reminyl prolonged release	Galantamine	Capsule	Extended release
Lescol XL	fluvastatin	Tablet	Extended release
Trufen Ultrafen Ibufen Isofen	Ibubrufen	Tablet	Taste (e)
Lamictal XR	Lamotrigen	Tablet	Extended release
-	Bisacodyl	Tablet	Enteric coated (c)
Janumet XR	Sitagliptin/Metformin	Tablet	Extended release

(a) Capsule may be opened and the contents taken without crushing or chewing; soft food such as applesauce or or pudding may facilitate administration; contents may generally be administered via nasogastric tube using an appropriate fluid providing entire contents are washed down the tube.

(b) Liquid dosage form of the product is available but dose, frequency of administration and manufactures may differ from that of the solid dosage form.

(c) Antiacid and or milk may prematurely dissolve the coating of the tablet.

(d) Capsule may be opened and the liquid contents removed from the administration.

(e) The taste of this product form would likely be unacceptable to the patient; administration via nasogastric tube would be acceptable.

(f) Effervescent tablet must be dissolved in the amount diluents recommended by the manufacturer.

(g) Tablets are made to disintegrate under the tongue.

(h) Tablet is scored and may be broken in half without affecting release characteristics.

(i) Skin contact may enhance tumor production avoid direct contact.

Note: This list is not meant to represent all products either by generic or trade name. The author encourages manufacturers, pharmacists, nurses and other health professionals to notify him of any changes or updates.

جامعة النجاح الوطنية

كلية الدراسات العليا

قياس المواقف و المعرفة والممارسة لمزاولي القطاع الصحي تجاه تجزئة او تفتيت الأشكال الدوائية الصلبة التي تعطى عن طريق الفم في فلسطين: السلامة والآثار العلاجية المترتبة على ذلك

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قدمت هذه الأطروحة استكمالا لمتطلبات الحصول على درجة الماجستير في الصيدلة السريرية، بكلية الدراسات العليا، في جامعة النجاح الوطنية، في نابلس–فلسطين.

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الملخص

المقدمة: يعتبر اعطاء او تناول حبوب الدواء مقسومة او مطحونة ممارسة شائعة بين مزودي الخدمات الصحية والمرضى ايضا وذلك لاسباب مختلفة، مثل: (أ) زيادة المرونة في اعطاء الجرعة. (ب) جعل اجزاء حبة الدواء اسهل للابتلاع. (ج) وايضا يجعل الدواء اقل كلفة. ولكن بالرغم من الفوائد المذكورة في الاعلى الا ان هذه الممارسة قد تكون خطيرة لان بعض التراكيب الدوائية وبعض اصناف الادوية غير مناسبة للطحن او التقسيم مما قد يسبب مشاكل خطيرة.

هدف الدراسة: الهدف من هذه الدراسة قياس المواقف و المعرفة والممارسة لمزاولي القطاع الصحي تجاه تجزئة او تفتيت الأشكال الدوائية الصلبة التي تعطى عن طريق الفم في فلسطين: السلامة والآثار العلاجية المترتبة على ذلك. بالاض **افة** الى ذلك تحديد العوامل التى تؤثر على مزودي الخدمات الصحية والتي تجعلهم يقومون بكسر او طحن الحبوب الصلبة. كما تهدف هذه الدراسة الى تحديد الاختلافات في المعرفة والمواقف بين المرضين والصيادلة.

طريقة البحث: تم اجراء دراسة مسحية على مستوى الوطن شملت مزودي الخدمات الصحية من ممرضين وصيادلة وتم اختبار المعرفة والمواقف والممارسة استبيان شمل اسئلة اختيار متعدد تم تصميمها خصيصا لهذا الغرض. وتم تجريب اسئلة الاستبيان سابقا والتحقق منها وتم تجميع النتائج وتحليلها.

نتائج الدراسة: تم توزيع 615استبيان اكتمل منها استبيان. توصلت الدراسة الى ان 67.3% من الصيادلة و5.6% من الممرضين لديهم مستويات معرفة جيده. كما ان 96% من الصيادلة و 36.4% من الممرضين لديهم مواقف جيده تجاه هذا الموضوع. اظهرت الدراسة ان هناك علاقة ايجابية بين مستويات المعرفة والمواقف فيما يخص الصيادلة والممرضين. اظهرت الدراسة ايضا ان 83.7% من الصيادلة و 43.6% من الممرضين لديهم ممارسة جيده.

الخلاصة: اظهرت هذه الدراسة ان هناك نقصا في المعرفة لدى ممارسي الخدمات الصحية وخصوصا الممرضين تجاه تجزئة اوتفتيت الحبوب الصلبة مما يؤثر ذلك على ممارستهم ومواقفهم تجاه هذا الموضوع. لذلك فانه يجب وضع خطط تطويرية وبرامج تدريبية بهدف تحسن المعرفة ورفع الكفاءة.