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ORIGINAL ARTICLE

Medications that should not be crushed

S.L. Gracia-Vásquez*, P. González-Barranco, I.A. Camacho-Mora, O. González-Santiago, S.A. Vázquez-Rodríguez

Universidad Autonoma de Nuevo Leon, UANL, Facultad de Ciencias Químicas, San Nicolás de los Garza, Nuevo León, México

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Abstract
Goal: To evaluate the knowledge about medications that could or could not be crushed or split among a group of patients in the Monterrey metropolitan area, and make a list of medications available in México that should not be crushed or split.
Material and methods: A descriptive, observational, transverse study was conducted using validated surveys among 950 patients undergoing medical treatment that went to clinics in the cities of San Nicolás de los Garza, Monterrey and Guadalupe of the Monterrey metropolitan area. The survey included a series of questions aimed at learning the patients' level of knowledge regarding which drugs can be split or crushed. In order to collect the list of medications, several databases were consulted.
Results: Of the study group, 80.3% had crushed or split a tablet prior to its administration, most of them to facilitate oral intake. Fifty four percent (54.4%) did not ask their physicians about this procedure. Seventy two (72.5%) percent considered that not all tablets should be crushed, but they did not know the exact reason why. An extensive list of medications available on the Mexican market that should not be crushed or split was presented.
Conclusions: There is an urgent need to improve the information available regarding what dosage forms can be split or crushed in order to prevent medication errors.

Introduction

According to the World Health Organization (WHO), health is defined not only as the absence of disease, but also as a state of physical, psychological and social well-being as an individual, as well as collectively. Thus, the concept of public health acknowledges the fact that health worker

* Corresponding author at: Universidad Autonoma de Nuevo Leon, UANL, Facultad de Ciencias Químicas, Av. Universidad S/N, Ciudad Universitaria, San Nicolás de los Garza, Nuevo León CP 66455, México. Tel.: +52 8329 4000.
E-mail address: sandra.graciavs@uanl.edu.mx (S.L. Gracia-Vásquez).

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interventions include not only clinical services, which focus mostly on somatic and psychological aspects, but also social interventions such as production, rent distribution, consumption, housing, work, environment, etc.[1]

On the other hand, the irrational use of medications is also a public health concern and a major problem worldwide. This problem has been detected, and international organizations such as the WHO have developed different projects and guidelines to reduce it.[2] Rational use of medications require that the patients receive the correct medications, each according to their clinical needs, as well as the correct dose and for the proper period of time, all this at the lowest possible cost for the patients and their communities.[3] Public education on this subject is fundamental, since the vast majority of medications are prescribed by a physician, including dosage, frequency, length of treatment and the correct method of administration; and even if a pharmacist were able to solve all the patient's questions on common administration practices and the best hours to take the medications, it is the patient who decides whether or not to follow those instructions, basing his/her decision on a complex set of family beliefs, social, economic and health factors. The patient decides whether or not to buy the medication, take the right doses at the correct frequency, and take it as indicated or split it, especially when dealing with over-the-counter medications. Being well-informed is considered a right for the patient, but it is also an obligation for them to actively participate in the care of their well-being in conjunction with health care professionals.[3,4]

As a part of a pharmaceutical treatment, splitting (cutting in half) or crushing medications has been an accepted practice as a way of obtaining the prescribed dose when a specific dose is not available. For example, in pediatric or geriatric patients for whom, more often than not, the proper doses are not available on the market. Other examples include cases where there is a need to provide proper fractioned doses within a flexible regimen, when there is a need to reduce or increase the dosage in a dosing regimen, when there is a need to begin therapy with the lowest possible dose in order to avoid an incidence of adverse effects, when there is a need to adjust the therapeutic response of an individual patient, as an aid in the administration of large tablets which patients find hard to swallow whole, and as a way of saving using cheaper larger dose medications in the required proportions.[5–14]

However, there are pharmaceutical dosage forms which, in principle, should never be crushed. Amongst these are those that come with an enteric coating used for drugs which are inactivated by gastric acid, or that could irritate gastric mucous and used for delayed release. Other dosage forms which should never be crushed are those for sublingual administration, these are designed so that the drug dissolves quickly for a better absorption, thus reaching the bloodstream in a shorter period of time. Certain tablets with a polymeric or sugar coating which disguise unpleasant flavors and smells that avoid mucous irritation or protect active ingredients which are affected by light or humidity should also not be crushed or split, as well as effervescent or dispersible pharmaceutical dosage forms which are designed to dissolve or disperse in water before ingestion; if these are chewed, they could lose their ability to dissolve quickly, thus possibly causing a loss of dosage, in addition to presenting effervescence in the mouth if it is not dissolved in water first. Soft gelatin capsules (with liquid content) should also not be chewed or split, since the extraction of the liquid inside may lead to an incorrect dosage. In the case of medications with prolonged or extended released, if the developed system which contains the dose is destroyed, incidence of collateral side effects or the toxicity of the medication may increase when releasing a greater dose of the active ingredient.[15–18] Other formulations which may present problems when crushed are medications with carcinogenic potential, not because their pharmacokinetic characteristics are modified, but because of the risk that tampering with it involves. Some active ingredients like warfarin or levothyroxine have small therapeutic windows; that is to say, if split in uneven parts and ingested, elevated doses of the medication are obtained for immediate absorption and can potentially cause toxicity, or result in a dosage which is under the therapeutic dose.[5,19–23]

The objective of this study was to evaluate the knowledge of a group of patients in Monterrey, Nuevo León, México and its metropolitan area has about oral medications that should not be split or crushed, and to gather commercial names of medications on the Mexican market which should not be altered.

Material and methods

An observational, transversal, descriptive study was conducted through a previously validated survey. The surveys were applied to those patients who were on medical treatment at that moment and visited clinics and hospitals located in Monterrey, San Nicolas and Guadalupe, both cities located in the metropolitan area of Monterrey, Nuevo Leon, México. Pharmacists were in charge of conducting the survey, and the surveys were applied between July and December of 2015. All patients provided a signed consent prior to the application of the instrument. In the case of minors, their guardians provided said consent. The survey included a series of questions aimed at understanding the degree of knowledge patients had about which medications could be split and/or crushed.

The instrument was developed by experts in the area after a thorough bibliographic review. The items were then evaluated by an expert panel in the field of assistential pharmacy with a doctoral degree in Pharmacy, and finally, these evaluated questions were first applied to a small population group that was given a close follow-up to see if they fully understood each of the questions and once any situations found were corrected, a survey was applied to a pilot group close to the target population of our survey (30 patients), i.e. patients in the metropolitan area of Monterrey. Once this was done, the validated survey was applied to the population described. The responses to the survey were stored in a database and processed in Excel. Descriptive statistical analysis was performed. For the compilation of the list of medicines that should not be splitted or crushed, consultations were carried out from various sources of up-to-date information, such as scientific articles of indexed journals, as well as secondary bibliographic sources, specifically PubMed, EBSCO, and LexiComp, and tertiary sources

Table 1 Demographics of the population.

Characteristic	Frequency (%)
Gender	
Male	444 (46.7)
Female	506 (53.3)
Age range	
10–29	431 (45.4)
30–49	383 (40.3)
50–69	127 (13.4)
70–89	9 (0.9)
Average	32.0
Average ± SD	33.8 ± 13.6
Schooling level	
None	12 (1.3)
Elementary	88 (9.3)
Junior high	257 (27.0)
High school	427 (45.0)
Bachelor's	137 (14.4)
Postgraduate	29 (3.0)
Employment status	
Working	746 (78.5)
Not working	204 (21.5)

N = 950; SD, standard deviation.

such as books of pharmaceutical technology and dictionaries of pharmaceutical specialties, among others.

Results

The study involved 950 people from different communities in the metropolitan area of Monterrey, N.L., México; their demographic characteristics are shown in Table 1.

Results showed that 80.3% reported having split or crushed a tablet prior to administration, the main reason (49.8%) being to facilitate administration and swallowing, followed by an indication by the physician (20.0%), to adjust the dose (22.0%), to disguise a bad taste (7.2%), and 1.0% of the respondents mentioned another reason. The most frequently used instrument (50%) for splitting the tablets was a knife, followed by the hands (29%), the teeth (11%), and finally a splitter (10%) (Fig. 1).

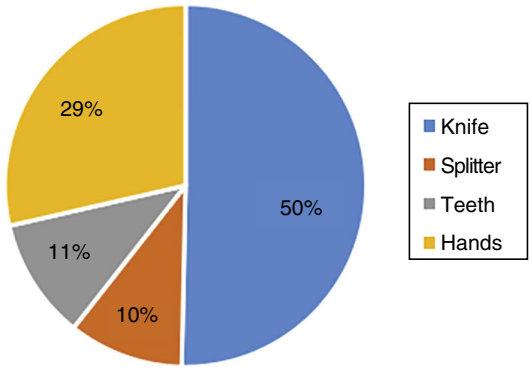

Figure 1 Instruments most commonly used to split tablets.

Table 2 Reasons not to split medications.

Motive	Frequency (%)
Loss of drug effect	380 (40.0)
Bad taste	209 (22.0)
Irritation of the stomach	190 (20.0)
Extended or prolonged released medications	68 (7.2)
Possibility of toxicity	19 (2.0)
Other reasons	84 (8.8)

n = 950.

Most respondents (72.5%) considered that not all medicines can be splitted or crushed, and when questioned about why, the most common response was the fact that it could cause the drug to have no effect (40.0%); other reasons are shown in Table 2.

Further results show that 54.4% did not consult a physician before carrying out this practice. A large part of the respondents, 895 people (94.2%), were interested in knowing more about medications that could or could not be split in two or crushed, and would like to receive this information from a health professional.

Moreover, 49% of the respondents reported having had some discomfort when ingesting a split tablet, the most frequent being stomach irritation. Forty nine percent (49.6%) said that the main consequence of crushing tablets is the bitter taste that may occur and some less common ones would be: oral mucosal irritation, toxicity, dose inaccuracy and dental staining.

Table 3 lists orally administered medications that should not be crushed or splitted, thereby avoiding side effects, toxicity or inefficacy caused by this practice. Although the list is numerous and serves as a guide for health professionals in México, there are other medicines on the market that are not listed.[19,24–26]

Discussion

Our study reveals that a large proportion of patients (80.3%) who have used tablets as a pharmaceutical form of drug administration have splitted them or crushed them, unlike the study by Quinzler et al., in which 49% of its study population split at least one drug.[8] The latter results resemble a study carried out in the Netherlands at five community pharmacies, where 31% of tablet prescriptions were found to have been modified prior to administration; that is, they were splitor crushed because the prescribed dose needed to be reduced; 30% were split on the initiative of the patient, 13% because of the ease of administration and 17% because the patient chose to take a lower dose.[20] In the present study, about 50% of the patients stated that the main reason was for ease of administration, while 22% stated that their reason was dose adjustment. Despite the differences in the results of the cited research and the present study, according to Rodenhuis et al., there is an important need for patients to cover these two aspects.[20]

Although the practice of splitting tablets is common both in outpatient settings and in hospitals and nursing

Table 3 Oral medications that should not be splitor crushed.

Commercial name	Generic name	Pharmaceutical dosage form	Reasons or comments
ABBATIN	Montelukast sodium	Tablets	Coated
ACORTRAL	Sertraline hydrochloride	Tablets	Coated
ACXION AP	Phentermine hydrochloride	Tablets	Prolonged release
ADALAT OROS	Nifedipino	Tablets	Prolonged release
AFINITOR	Everolimus	Tablets	Do not chew or crush By manufacturer
AGIOLAX	Plantago ovata Senna angustifolia	Granules	Coated
AGRIXAL	Omeprazole	Capsules	Enteric coating[c]
AKINETON DELAYED	Biperidene hydrochloride	Tablets	Prolonged release
AMARLY XM	Glimepiride Metformin hydrochloride	Tablets	Prolonged release
ANGELIQ	Estradiol Drospirenone	Tablets	Coated
ANGIOTROFIN DELAYED	Diltiazem hydrochloride	Tablets	Prolonged release
ANTAGIN	Indomethacin	Capsules	Prolonged release
ARCALION	Sulbutylamine	Tablets	Coated
ARCOXIA	Etoricoxib	Tablets	Coated
ASA 100	Acetylsalicylic acid	Tablets	Prolonged release[d]
ASACOL	Mesalazine	Tablets	Delayed release
ASOFLON	Tamsulosin	Capsules	Controlled release
ASPIRIN PROTECT	Acetylsalicylic acid	Tablets	Enteric coating[c]
ATEMPERATOR	Magnesium valproate	Tablets	Enteric coating[c]
ATEMPERATOR LP	Magnesium valproate	Tablets	Prolonged release
ATHOS	Dextromethorphan hydrobromide	Capsules	Prolonged release
ATRIPLA	Efavirenz Emtricitabine Tenofovirdisoproxilfumarate	Tablets	Coated
AVADEN	Estradiol Gestodeno	Tablets	Prolonged release
AVODART	Dutasteride	Capsules	Liquid filling[k]
BEDOYECTA	Vitamins: C, B1, B2, B6, B12 Folic acid	Capsules	Liquid filling[e]
BENEDORM	Melatonin	Tablets	Sublingual[h]
BIOMESIN COMPOUND	Hyoscine butylbromide Metamizole sodium monohydrate	Tablets	Coated
BI-PROFENID	Ketoprofen	Tablets	Prolonged release[g]
BOREALIS	Finasteride	Tablets	Coated
BROSPINA SL	Buprenorphine hydrochloride	Tablets	Sublingual[h]
BRUNACOL	Ketorolac tromethamine	Tablets	Coated
BUSCAPINA COMPOSITUM	Butylhioscinbromide Sodium metamizole monohydrate	Tablets	Coated
CAPRELSA	Vandetanib	Tablets	Coated
CASDROGEN	Bicalutamide	Tablets	Do not chew By manufacturer
CECLOR 12 H	Cefaclormonohydrate	Tablets	Prolonged release[g]
CECLORDOX	Cefaclor Bromhexine hydrochloride	Tablets	Prolonged release[g]
CEFABIOT	Cefuroxime axethyl	Tablets	Coated

Table 3 (*Continued*)

Commercial name	Generic name	Pharmaceutical dosage form	Reasons or comments
CEFURACET	Axetilcefuroxime	Tablets	Coated
CEPACAÍNA	Cetylpyridinium chloride Benzocaine	Lozenge	Do not chew Local action
CEPACOL	Cetylpyridinium chloride	Lozenge	Do not chew Local action
CERTICAN	Everolimus	Tablets	Do not break By manufacturer
CERVILAN	Lomifilina Dihydroergocristinemesylate	Coated Tablets	Coated[c]
CIALIS	Tadalafil	Tablets	Coated
CIPROFLOX DM	Ciprofloxacin hydrochloride hydrochloride	Tablets	Prolonged release
CIPROXINA	Ciprofloxacin hydrochloride monohydrate	Tablets	Do not break By manufacturer
CIPRO XR	Ciprofloxacin hydrochloride	Tablets	Prolonged release
CITOX	Citalopram hydrobromide	Tablets	Coated
CLARITYNE D	Loratadine Phenylephrine hydrochloride	Tablets	Sustained release
COMBODART	Dutasteride Tamsulosin hydrochloride	Capsules	Mucosal irritation
CONCOR	Bisoprolol fumarate	Coated tablets	Coated
CONTROLIP	Fenofibrate	Capsules	Swallow whole By manufacturer
CORPOTASIN CL	Potassium bicarbonate Potassium chloride Lysine hydrochloride	Tablets	Effervescent[f]
CORPOTASIN LP	Potassium chloride	Tablets	Prolonged release
CREON	Pancreatin	Capsules	Microspheres with enteric coating[c]
CRIAM PROLONGED RELEASE	Magnesium valproate	Tablets	Prolonged release[g]
CRONOCAPS	Melatonin	Capsules	Prolonged release
CYMBALTA	Duloxetine hydrochloride	Capsules	Delayed release
DABEX XR	Metformin hydrochloride	Tablets	Prolonged release
DAGLA	Itopride hydrochloride	Tablets	Coated
DANZEN	Serratiopeptidase	Tablets	Enteric coating[c]
DAXON	Nitazoxanide	Tablets	Dispersable[i]
DAXXAS	Roflumilast	Tablets	Coated
DEBEONE DT NF	Metformin hydrochloride	Tablets	Prolonged release
DEPAKENE	Valproic acid	Capsules	Mucosal irritation
DEXIDEX	Nitazoxanide	Tablets	Coated
DEXIVANT	Dexlansoprazole	Capsules	Delayed release
DIAMICRON MR	Glycazide	Tablets	Prolonged release
DIANE	Cyproterone Ethinylestradiol	Coated tablets	Coated
DICETEL	Pinaverium bromide	Tablets	Coated
DILACORAN DELAYED	Verapamil	Tablets	Prolonged release

Table 3 (*Continued*)

Commercial name	Generic name	Pharmaceutical dosage form	Reasons or comments
DIMEFOR-G	Metformin hydrochloride Glibenclamide	Tablets	Coated[b]
DIMEGAN-D	Loratadine Phenylephrine hydrochloride	Capsules	Prolonged release
DINORAX	Metformin hydrochloride	Tablets	Coated
DINORAX C	Metformin hydrochloride Glibenclamide	Tablets	Coated
DIURMESSEL	Furosemide	Tablets	Do not break By manufacturer
DOLAC 30	Ketorolac tromethamine	Tablets	Sublingual
DOLFLAM-RETARD	Diclofenac sodium	Coated tablets	Prolonged release
DOLOCAM	Meloxicam	Tablets	Sublingual[h]
DORIXINA RELAX	Lysine clonixinate Cyclobenzaprine hydrochloride	Tablets	Coated
DOYCUR	Clarithromycin	Tablets	Coated
DUCICLON	Diclofenac sodium Vitamins: B1, B6, B12	Coated tablets	Coated
DUPLAT	Pentoxifylline	Coated tablets	Coated
DUSPATALIN	Mebeverina	Capsules	Prolonged release
EBIXA	Memantine hydrochloride	Tablets	Do not break By manufacturer
EFFIENT	Prasugrel	Tablets	Coated[a]
EMSELEX	Darifenacine bromide	Tablets	Prolonged release
ENDOCODIL XR	Oxycodone hydrochloride	Tablets	Prolonged release
ENTOCORT	Budesonide	Capsules	Prolonged release
EPIVAL	Valproate semisodium	Tablets	Enteric coating[c]
EPIVAL ER	Valproate semisodium	Tablets	Prolonged release
EPRATENZ DOX	Eprosartan hydrochlorothiazide	Tablets	Coated
ESBELCAPS	Fenproporex hydrochloride Diazepam	Capsules	Prolonged release
ESCAPIN-N	Butylphoscinebromide Paracetamol	Coated tablets	Coated
ESPAVEN ENZIMÁTICO	Pancreatin Ox bile extract Dimethicone Cellulase	Coated tablets	Enteric coating[c]
EVADOL	Diclofenac sodium	Coated Tablets	Coated[c]
FEPROREX	Fenproporex hydrochloride	Capsules	Prolonged release
FERROTEMP	Ferrous fumarate Thiamine mononitrate	Capsules	Prolonged release
FLONORM	Rifaximin	Coated Tablets (Dragee)	Coated
FLOXACIN	Norfloxacin	Tablets	Coated
FORCEDOL	Tramadol hydrochloride Ketorolac tromethamine	Tablets	Sublingual
FOSAMAX PLUS	Alendronate sodium Colecalciferol	Tablets	Mucosal irritation

Table 3 (*Continued*)

Commercial name	Generic name	Pharmaceutical dosage form	Reasons or comments
FOSFONAT	Ibandronic acid	Tablets	Mucosal irritation
FOTORAL	Vitamins and minerals	Capsules	Liquid filling[e]
FRAVITAN	Vitamins and minerals	Capsules	Liquid filling
GALEDOL	Diclofenac sodium	Coated Tablets	Prolonged release
GALEDOR	Diclofenac sodium	Tablets	Effervescente[f]
GIMACLAV	Amoxicillin potassium clavulanate	Tablets	Coated
GLIMETAL LEX	Glimepiride Metformin hydrochloride	Tablets	Prolonged release
GLUPROPAN	Glimepiride	Tablets	Produces unpleasant taste
HYZAAR	Losartan potassium Hydrochlorothiazide	Tablets	Coated[g]
ILIMIT	Drospirenone Ethinylestradiol	Tablets	Coated
IMDUR	Isosorbide mononitrate	Tablets	Prolonged release
IMPAZA	Endothelial anti-NO-synthase polyclonal antibody	Tablets	Orodispersable
IRESSA	Gefitinib	Tablets	Sublingual[h]
ISENTRESS	Potassium raltegravir	Tablets	Coated[b]
ISMIGEN	Freeze-dried bacterial lysate	Tablets	Sublingual[h]
ISORBID	Isosorbide dinitrate	Tablets	Sublingual[h]
ISORBID A.P	Isosorbide dinitrate	Capsules	Prolonged release
ITALNIK	Ciprofloxacin hydrochloride	Tablets	Prolonged release
ITRAVIL AP	Clobenzorex hydrochloride	Tablets	Prolonged release
JUMSLIM	Tamsulosin hydrochloride	Capsules	Prolonged release
KALETRA	Lopinavir Ritonavir	Tablets	Coated
KALIOLITE	Potassium chloride	Coated tablets	Coated[c]
KEPPRA XR	Levetiracetam	Tablets	Prolonged release
KIVEXA	Abacavir sulfate Lamivudine	Tablets	Coated
KLARICID O.D.	Clarithromycin	Tablets	Prolonged release
KOMBIGLYZE XR	Saxagliptin Metformin hydrochloride	Tablets	Prolonged release
KYTRIL	Granisetron hydrochloride	Coated tablets	Coated
LACDOL-S	Ketorolac tromethamine	Tablets	Sublingual[h]
LEFLOXIN	Levofloxacin hemihydrate	Tablets	Coated
LEGALON	Silymarin	Coated tablets	Coated
LODESTAR	Losartan potassium	Tablets	Coated
LODESTAR ZID	Losartan potassium Hydrochlorothiazide	Tablets	Coated
LOGIMAX	Felodipino Meproprololsuccinate	Tablets	Prolonged release
LOSECA	Omeprazole	Capsules	Prolonged release
LUVOX	Fluvoxamine maleate	Tablets	Coated
LYSOMUCIL	Acetylcysteine	Tablets	Effervescent[f]

Table 3 (*Continued*)

Commercial name	Generic name	Pharmaceutical dosage form	Reasons or comments
MACRODANTINA	Nitrofurantoin	Capsules	Prolonged release
MAVIGLIN	Metformin hydrochloride Glibenclamide	Coated tablets	Coated
MAZDA	Venlafaxine hydrochloride	Capsules	Prolonged release
MESTINON TIMESPAN	Pyridostigmine bromide	Tablets	Prolonged release
MICARDIS	Telmisartan	Tablets	Prolonged release
MICROGYNON CD	Levonorgestrel Ethinylestradiol	Coated tablets	Coated
MICROLUT	Levonorgestrel	Coated tablets	Coated
MICROMYCIN	Minocycline hydrochloride	Capsules	Controlled release[d]
MICTASOL	Norfloxacin Phenazopyridine chlorhydrate	Tablets	Do not break By manufacturer
MONOCRAT DEPOT	Isosorbide mononitrate	Tablets	Prolonged release
NATRILIX SR	Indapamide	Tablets	Prolonged release
NEDICLON	Diclofenac sodium	Coated tablets	Prolonged release
NEOBES	Amfepramone hydrochloride	Capsules	Prolonged release
NEOGYNON	Levonorgestrel Ethinylestradiol	Coated tablets	Coated
NEO-MELUBRINA	Sodium metamizole	Tablets	Effervescent
NEPTALIP EXTENDED	Bezafibrate	Tablets	Prolonged release
NEUGERON LP	Carbamazepine	Tablets	Prolonged release
NEUPAX	Alprazolam Sulpiride	Tablets	Sublingual[h]
NEXIUM-MUPS	Esomeprazole magnesium trihydrate	Tablets	Coated[j]
NIFEZZARD	Nifedipino	Capsules	Liquid filling[e]
NORVIR	Ritonavir	Tablets	Mucosal irritation
OBECLOX LP	Clobenzorex	Tablets	Prolonged release
OGASTRO	Lansoprazole	Capsules	Coated[j]
OMACOR	Ethyl esters of omega-3 fatty acids	Capsules	Liquid filling[e]
ONEMER	Ketorolac tromethamine	Tablets	Coated
ONEMER SL	Ketorolac tromethamine	Tablets	Sublingual[h]
ONOTON	Pancreatin Hemicellulase Simethicone	Tablets	Enteric coating[c]
OPORTUNA	Levonorgestrel	Coated tablets	Coated[a]
OSSOPAN	Calcium Phosphorus Protein	Coated tablets	Coated[a]
PALATRIN	Lansoprazol	Tablets	Enteric coating[c]
PALEXIA DELAYED	Tapentadol hydrochloride	Tablets	Prolonged release
PANKREOFLAT	Pancreatin Dimethicone	Tablets	Enteric coating[c]
PANTOZOL	Pantoprazole sodium sesquihydrate	Granules	Coated[j]
PARAMIX	Nitazoxanide	Coated tablets	Coated[a]

Table 3 (*Continued*)

Commercial name	Generic name	Pharmaceutical dosage form	Reasons or comments
PARAMIX	Nitazoxanide	Tablets	Dispersable[i]
PAXIL	Paroxetine hydrochloride	Tablets	Do not break By manufacturer
PAXIL CR	Paroxetine hydrochloride	Tablets	Prolonged release
PENTASA	Mesalazine	Tablets	Prolonged release
PENTASA	Mesalazine	Granules	Prolonged release[d]
PHENODICAL	Felodipino	Tablets	Prolonged release
PHLOGENZYM	Bromelain Trypsin Routine	Coated tablets	Coated[c]
PLANTIVAL	Valeriana officinalis Melissa officinalis	Coated tablets	Coated[a]
PLASIL ENZYMATIC	Metoclopramide Bromelain Dimethicone Pancreatin Sodium dehydrocholate	Coated tablets	Coated[a]
PLENACOR LP	Atenolol Nifedipino	Capsules	Prolonged release
PLENDIL	Felodipino	Tablets	Prolonged release
POSIPEN	Dicloxacillin sodium	Tablets	Prolonged release
PREDIAL PLUS	Metformin hydrochloride	Tablets	Prolonged release
PREDXAL PLUS	Telmisartan Hydrochlorothiazide	Tablets	Do not break By manufacturer
PRENATEX	Vitamins Minerals	Coated tabletss	Coated
PRETERAX	Perindopril arginine Indapamide	Tablets	Coated
PRILIGY	Dapoxetine hydrochloride	Tablets	Coated
PRIMOGYN	Estradiol valerate	Coated tablets	Coated
PROBITOR	Anastrozole	Tablets	Coated[b]
PROCORALAN	Ivabradine hydrochloride	Tablets	Coated[b]
PROGRAF XL	Tacrolimus monohydrate	Capsules	Prolonged release
PRONTOFORT	Tramadol hydrochloride	Capsules	Prolonged release
PROPESHIA	Finasteride	Coated tablets	Coated[a]
PROTALGINE	Lamotrigine	Tablets	Dispersable[i]
PROVAY	Ciprofloxacin hydrochloride monohydrate	Tablets	Coated
PROZAC 20 DISPERSABLE	Fluoxetine hydrochloride	Tablets	Dispersable[i]
PULSARAT	Simvastatin	Tablets	Coated[b]
PYLOPAC	Lansoprazole Clarithromycin Amoxicillin	Tablets	Coated
QUEDOX	Clarithromycin	Tablets	Coated
RANTUDIL DELAYED	Acemetacin	Capsules	Coated[j]
RAPIX	Ketorolac tromethamine	Tablets	Sublingual[h]
RAYPID	Gemfibrozil	Tablets	Coated[b]
REDOTEX	D-norpseudoephedrine hydrochloride Triiodothyronine sodium Atropine sulfate Aloin Diazepam	Capsules	Prolonged release

Table 3 (*Continued*)

Commercial name	Generic name	Pharmaceutical dosage form	Reasons or comments
REDOTEX NF	D-norpseudoephedrine hydrochloride Atropine sulfate Aloin	Capsules	Prolonged release
RENAGEL	Sevelamer hydrochloride	Tablets	Coated[b]
RESOTRANS	Prucalopride succinate	Tablets	Coated
REVLIMID	Lenalidomide	Capsules	Should not be opened or chewed By manufacturer
RIFAPRIM	Rifampicin Trimethoprim	Coated tablets	Coated
RIFATER	Rifampicin Isoniazid Pyrazinamide	Coated tablets	Coated[a]
RIXTAL	Itraconazole	Capsules	Should be swallowed, do not open By manufacturer
SALOFALK	Mesalazine	Tablets	Enteric coating[c]
SAMYR	1,4 Butane adenosine disulfonate	Tablets	Do not break By manufacturer
SECOTEX	Tamsulosin hydrochloride	Capsules	Prolonged release
SECOTEX OCAS	Tamsulosin hydrochloride	Tablets	Prolonged release
SELOKEN ZOK	Meproprololsuccinate	Coated tablets	Coated[d]
SELOPRES ZOK	Meproprololsuccinate Hydrochlorothiazide	Tablets	Coated[d]
SENOVITAL	Montelukastsodium	Tablets	Coated
SENSIBIT	Loratadine	Tablets	Orodispersable[n]
SERITRAL	Itraconazole	Capsules	Should be swallowed, do not open By manufacturer
SERONEX LP	Domperidona	Tablets	Prolonged release
SEROQUEL XR	Quetiapine	Tablets	Prolonged release
SERVAMOX CLV	Amoxicillin trihydrate Potassium clavulanate	Tablets	Coated
SIFROL ER	Pramipexole dichlorhydrate	Tablets	Prolonged release
SINCRONIUM	Acetylsalicylic acid Simvastatin Ramipril	Capsules	Should be swallowed, do not open By manufacturer
SINERGIX	Tramadol hydrochloride ketorolac tromethamine	Tablets	Sublingual[h]
SINGULAIR	Montelukastsodium	Tablets	Coated[b]
SIRDALUD MR	Tizanidine hydrochloride	Capsules	Prolonged release
SOLUCAPS	Mazindol	Capsules	Prolonged release
SOMAZINA	Citicolinasodium	Tablets	Coated
SOMERAL	Alpha keto analogs of amino acids	Coated tablets	Coated[a]
SPECTRACEF	Cefditorenpivoxil	Tablets	Coated
STALEVO	Entacapone Levodopa Carbidopa monohydrate	Tablets	Coated[b]

Table 3 (*Continued*)

Commercial name	Generic name	Pharmaceutical dosage form	Reasons or comments
STELABID	Trifluoperazine dihydrochloride Isopropamide iodide	Coated tablets	Coated[a]
STILNOX CR	Tartrate of zolpidem	Tablets	Prolonged release
SUB-Z	Melatonin	Tablets	Sublingual[h]
SUFISAL	Pentoxifylline	Coated tablets	Prolonged release
SUPACID	Pantoprazole sodium sesquihydrate	Tablets	Prolonged release
SUPRADOL	Ketorolac tromethamine	Tablets	Sublingual[h]
TARDYFERON FOL	Ferrous sulfate Folic acid	Coated tablets	Prolonged release
TARKA	Trandolapril Verapamil hydrochloride	Tablets	Do not break By manufacturer
TEBONIN OD	Dry extract of ginkgo biloba	Tablets	Prolonged release
TEGRETOL LC	Carbamazepine	Tablets	Prolonged release
TEMPOLIB	Trimebutine maleate	Tablets	Prolonged release
TEOLONG	Theophylline	Capsules	Prolonged release[d]
TESAPERL	Benzonatato	Capsules	Liquid filling[e]
TEVETENZ	Eprosartanmesylate	Tablets	Coated[b]
TEVETENZ DOX	Eprosartanmesylate Hydrochlorothiazide	Tablets	Coated[b]
THIOCTACID 600HR	Thiotic acid	Tablets	Do not break By manufacturer
TIBACLIM	Tibolona Calciumcarbonate Colecalciferol (vitamin D_3)	Tablets	Coated
TOLORAN	Ketorolac tromethamine	Tablets	Sublingual[h]
TOLVON	Miaserin	Tablets	Should be ingested without chewing
TRACLEER	Bosentan monohydrate	Tablets	Coated
TRADOL	Tramadol hydrochloride	Capsules	Should be swallowed, do not open By manufacturer
TRADEA	Methylphenidate hydrochloride	Tablets	Prolonged release
TRADOL DELAYED	Tramadol hydrochloride	Tablets	Prolonged release
TRANKITEC	Magnesium valproate	Tablets	Coated[c]
TRANSKRIP	Magnesium valproate Hydralazine hydrochloride	Tablets	Prolonged release
TRIBEDOCE COMPOUND	Diclofenac sodium Thiamine mononitrate Pyridoxine hydrochloride Cyanocobalamin	Coated tablets	Coated[a]
TRIQUILAR	Levonorgestrel Ethinylestradiol	Coated tablets)	Coated
TRUVADA	Emtricitabine Tenofovir disoproxil fumarate	Tablets	Coated[b]
TYKERB	Lapatinib	Tablets	Coated
ULCEVIT	Ranitidine hydrochloride	Coated tablets	Coated[a]

Table 3 (*Continued*)

Commercial name	Generic name	Pharmaceutical dosage form	Reasons or comments
ULGASTRIN	Ranitidine hydrochloride	Coated tablets	Coated[a]
ULPAX	Lansoprazole	Capsules	Delayed release
ULSEN	Omeprazole	Capsules	Coated[j]
ULSEN PCS	Omeprazole	Capsules	Coated[j]
VANTOXYL	Pentoxifylline	Tablets	Prolonged release
VICTAN	Ethyl loflazepate	Tablets	Coated[b]
VIMOVO	Naproxen Esomeprazole	Tablets	Delayed release
VIVIOPTAL	Vitamins Minerals	Capsules	Liquid filling[e]
VOLFENAC DELAYED	Diclofenac sodium	Coated tablets	Prolonged release
VOLTAREN DOLO	Diclofenac potassium	Capsules	Do not break By manufacturer
WELLBUTRIN	Anfebutamona (Bupropion)	Tablets	Prolonged release
WOBE-MUGOS	Trypsin Chymotrypsin Papain	Coated tablets	Coated[c]
WOBENZYM	Proteolytic enzymes	Coated tablets	Coated[c]
XATRAL OD	Alfuzosinhydrochloride	Tablets	Prolonged release
XELODA	Capecitabine	Tablets	Coated
XUZAL	Levocetirizine dihydrochloride	Tablets	Do not break By manufacturer
ZALDIAR	Paracetamol Tramadol hydrochloride	Tablets	Effervescent[f]
ZAPEX	Mirtazapine	Tablets	Do not break By manufacturer
ZELBORAF	Vemurafenib	Tablets	Coated
ZITROFLAM	Nimesulide Azithromycin dihydrate	Tablets	Coated[b]
ZOMIG RAPIMELT	Zolmitriptan	Tablets	Dispersable[i]
ZYLOPRIM	Allopurinol	Tablets	Mucosal irritation
ZYPREXA ZYDIS	Olanzapine	Tablets	Dispersable[i]
ZYTIGA	Abiraterone	Tablets	Mucosal irritation

[a] Covered with sugar: masks smells and/or unpleasant flavors, protects photosensitive or easily oxidizable drugs.
[b] Coated with polymer film: masks odors and/or unpleasant flavors, protects photosensitive or easily oxidizable drugs, allows a prolonged release, depending on the coating polymer.
[c] Entericcoating: used for drugs that are destroyed by gastric acidity, for drugs that irritate the stomach mucose and for delayed release. They release their active substance into the small intestine.
[d] Granules with slow-release coating: used for slowly or steadily releasing the active substance.
[e] Capsules of soft gelatin (with liquid content): The extraction of the liquid from the interior can lead to an incorrect dosage.
[f] Effervescent: designed to dissolve in water before ingesting, if chewed they lose their ability to dissolve quickly, and may present effervescence in the mouth if not dissolved in water beforehand.
[g] Prolonged or extended release: If the developed system containing the dose is destroyed, the incidence of side effects or the toxicity of the drug is increased by releasing a higher dose.
[h] Sublingual: intended to the drug dissolves quickly, obtains a better absorption and reaches the bloodstream in a short time.
[i] Dispersible: designed to be dispersed in water before swallowing, if dissolved improperly, there may be a loss of dosage.
[j] Enteric coated granules: used for drugs that are not activated by gastric acidity, for those that irritate the stomach mucose and for a delayed release. They release their active substance into the small intestine.

homes, little is known about these patterns.[27] In this study, most of the people interviewed used a knife to split the tablets, followed by using the hands, then the teeth and finally a tablet cutter. Studies indicate that the use of these cutters to facilitate the division of tablets is rare, since their use is not common because they are not available in all pharmacies.[8] The study by Quinzler et al. reports that 16.3% of patients had problems with tablet division, of

which 70.1% solved it using a knife or other sharp object, and only 19.4% used a cutter to split the medication.[8]

The practice of crushing or splitting tablets by patients can lead to health problems, since not all tablets are suitable for this purpose. Splitting prolonged or extended-release tablets may result in increased side effects and a compromise in effectiveness, given the uncontrolled release of the active ingredient, or the latter may be impaired if it is contained in enteric coated tablets or has the potential to irritate the stomach.[6–8,28–32]

On the other hand, it is generally considered that if the manufacturer marks a dividing line on the tablet, that means that it is fit to split. However, this is not always the case, since there is a degree of inaccuracy in breaking them due to their shape, size or type of coating which results in pieces of different sizes that can lead to fluctuations in the administered dose, especially if this occurs with narrow therapeutic window drugs, such as digoxin and warfarin, unlike drugs with broad therapeutic ranges and long half-lives, in which dose fluctuations are unlikely to be clinically significant.[6,7,33] In the case of psychotropic drugs, the convenience of splitting tablets may result from clinical observation, since for patients like the elderly the prescription of complete tablets can result in over sedation in some cases. Thus, it is recommended that, if they are going to be divided by the patient, also consider the possible physical limitations, and that pharmacists give appropriate counseling regarding the necessary tools to do it the right way.[34,35]

Other studies reveal positive aspects of the practice of breaking tablets, such as the economic benefit that both the patient and health institutions generate by reducing their costs by up to 50%, due to the fact that the costs of the drugs frequently decrease when the dose is increased, independently of this.[11,13,36]

The decision to split tablets should be made after reviewing the relevant considerations. The following recommendations can be used as a guide.[6,26]

- Use liquid dosage forms of the same medicines. If they are not available, consult your pharmacist to determine if extemporaneous (compounding) preparations can be made. Occasionally, the injectable form of the medication can be used by placing the appropriate amount of medication in a liquid as a juice. This should be done after consulting the pharmacist to ensure there are no compatibility problems or changes in absorption of the active ingredient.
- Check the product information before recommending that it be broken or crushed.
- Use a tablet cutter to improve accuracy. However, patients should be instructed in their proper use.
- Advise patients about the proper storage of tablet fragments.

In conclusion, we found that there is an urgent need to improve information about which pharmaceutical forms can be splitted, divided or crushed. The work of pharmacists and health professionals is critical in educating patients about how prescribed drugs should be administered, as well as providing relevant information and indications, with emphasis on aspects related to their use, administration, and conservation, with the goal of avoiding medication errors. Pharmaceutical companies should more clearly label presentations of drugs so that patients can recognize those that should not be splitted or crushed.

Ethical disclosures

Protection of human and animal subjects. The authors declare that no experiments were performed on humans or animals for this study.

Confidentiality of data. The authors declare that no patient data appear in this article.

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