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Tablet splitting practice in Jordan

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Abstract

Objectives To investigate the practice of tablet splitting and the frequency of using different techniques for tablet splitting at outpatient pharmacies in Jordan.

Methods A structured questionnaire was used to interview adult patients who were prescribed at least one medication in a half-tablet dosage at two main outpatient pharmacies in the north of Jordan.

Key findings A total of 491 patients were interviewed. The most commonly split medication was aspirin 325 mg (38.1%) followed by warfarin 5 mg (3.3%). The most common reason for tablet splitting was physician's order (41.2%). Additionally, (24.0%) of respondents sometimes skipped their doses due to tablet splitting difficulties. The majority of participants ($n = 312$, 63.5%) used their hands to split tablets. More than a tenth of the participants discarded parts of their tablets when splitting did not result in equal parts from their perspective.

Conclusion Tablet splitting practice resulted in drug waste and medication non-adherence. Pharmacists are encouraged to educate other healthcare providers and patients about the practice of tablet splitting and when it is acceptable and when it is not.

Keywords Jordan; practice; tablet splitting; technique

Introduction

Tablet splitting is commonly encountered in pharmacy practice.^[1–3] Healthcare providers may recommend tablet splitting for several reasons which include reducing costs, adjusting doses or overcoming swallowing difficulties. However, this practice is not risk free; it can result in incorrect dose administration and splitting of medications that should not be split such as controlled release products.^[4]

Several studies have been conducted evaluating weight uniformity of half-tablets.^[5–8] Elliott *et al.* investigated eight frequently split narrow therapeutic index or critical dosage medications for weight uniformity. Of the eight studied medications, five failed to comply with the European Pharmacopoeia recommendations for half-tablet weight uniformity. In addition, the results showed significant difference in splitting accuracy performed by nurses compared to laypersons (P value 0.027) which may potentially affect treatment outcomes.^[5] In Jordan, a study was conducted evaluating weight uniformity of half-tablets of four medications available in the Jordanian market and investigated the effect of tablet characteristics on weight uniformity of half-tablets. Medications were warfarin 5 mg, digoxin 0.25 mg, phenobarbital 30 mg and prednisolone 5 mg and were split using a knife. The results showed that warfarin passed the weight uniformity test; however, digoxin, phenobarbital and prednisolone did not. The study concluded that tablet splitting can result in half-tablets that fail the US Pharmacopoeia (USP) criteria for weight uniformity which can be of clinical significance in the cases of narrow therapeutic index medications.^[8]

Several techniques are used to split tablets such as knives, tablet splitters, scissors and by hand. This variation in tablet splitting techniques can affect precision and accuracy of tablet splitting and result in inaccurate dosing. A study investigated three techniques of tablet subdivision: hand breaking, tablet splitter and kitchen knife.^[9] The results showed that hand breaking was not equivalent to a kitchen knife and tablet splitters in terms of accuracy and precision of splitting. The researchers recommended decreasing the need for

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tablet splitting when possible.^[9] Another study compared hand splitting and a tablet cutter with regard to the accuracy of splitting a low dose tablet (salbutamol 4 mg tablet).^[10] The researchers analyzed weight variation and drug content using a validated spectrophotometric method. The results showed that 15% of the samples from a tablet cutter and 25% of the samples from hand splitting fell outside USP specification for weight. Additionally, the variation in drug content between the two halves reached 21.3% in the case of tablets split by hand and 7.13% in the case of tablets split by a tablet cutter.^[10]

The main objective of this study was to investigate the practice of tablet splitting at outpatient pharmacies in Jordan as well as to investigate the frequency of using different techniques for tablet subdivision.

Methods

This was a prospective, descriptive cross-sectional study conducted at the outpatient pharmacies of King Abdulla University Hospital and Princess Basma Teaching Hospital. King Abdulla University Hospital is the largest hospital in the north of Jordan with a capacity of more than 600 beds. Princess Basma Teaching Hospital, also in the north of Jordan, has a capacity of more than 200 beds. The outpatient pharmacy at Princess Basma Teaching Hospital serves more than 200 000 patients per year. All adult patients (18 years and older) who were prescribed at least one medication in a half-tablet dosage form and attended the outpatient pharmacies during working hours were invited to participate in the study while they were waiting for their prescriptions to be filled. Those who agreed to participate had the research goals and methods explained to them. The study protocol was approved by the Jordan University of Science and Technology Institutional Review Board (Research Number 8/101/2016) on 15 December 2016 and the Committee of Ethics of Research on Humans at the Jordan Ministry of Health (Research Number MOHREC170044) on 23 March 2017.

A questionnaire was developed after extensive literature review and checked by specialists (four pharmacists) for face validity. The questionnaire was developed and conducted in Arabic, which is the native language in Jordan. The questionnaire constituted of two sections. The first section included questions about demographic details in addition to questions about the split medication dosages, dosage forms and scientific and brand names. The second section included questions about reasons for tablet splitting, splitting difficulties, participants' tablet splitting techniques and other related issues.

Two research assistants, who were trained to conduct interviews and administer questionnaires, conducted face-to-face structured interviews. The research assistants checked prescriptions at the dispensing site and approached adult patients who were prescribed at least one medication in a half-tablet dosage form and invited them to participate in the study. Data collection took place from April 2017 to September 2017.

In an attempt to improve clarity and limit response bias, the questionnaire was piloted in a small sample of 10

participants, and necessary modifications were subsequently made.

Data analysis and statistics

Data entry were double checked for all data. For each participant, one medication was included in the analysis to avoid duplication. The Statistical Package for Social Sciences (SPSS, version 17.0) software was used to analyse the data. Pearson's Chi-Square test was used to assess the association between variables, such as gender, age, educational status and medications being split and reasons for tablet splitting, tablet splitting difficulties and patients skipping doses due to tablet splitting difficulties. In order to decrease outliers, the data were re-categorized. For example, age was re-categorized into two categories: less than 50 years of age and 50 years or older. Educational status categories were re-categorized from five categories (illiterate, primary school, secondary school, community college, university education and graduate studies) into three categories (illiterate, school education, college or university education). Medications being split were re-categorized from the first 23 most commonly split medications and others into four categories: the first three most commonly split medications (aspirin 325 mg, warfarin 5 mg and levothyroxine 50 mg) and others. In addition, reasons for splitting were re-categorized from six categories (physician's order, unavailability of the prescribed dose, decreasing the dose, swallowing difficulties, saving money and others) into four categories (physician's order, unavailability of the prescribed dose, decreasing the dose and others). Furthermore, splitting technique was re-categorized from seven categories (by hand, kitchen knife, tablet splitter, teeth, scissors, combination of more than one technique and others) into four categories (by hand, kitchen knife, tablet splitter and others). A *P* value 0.05 (two-sided) was considered statistically significant.

Results

A total of 491 patients were interviewed where 265 (54.0%) were women. Data concerning participants' demographics are shown in Table 1.

Table 2 states the most commonly split medications by participants. The most commonly split medication was aspirin 325 mg ($n = 187$, 38.1%) followed by warfarin 5 mg ($n = 16$, 3.3%). More than a quarter of the split medications (27.5%) were in the category 'Others', such as metformin 850 mg, bisoprolol 5 mg and amlodipine 10 mg. Moreover, split medications included controlled release formulations, for example, metoprolol 100 mg (Betaloc ZOK[®] 100 mg, $n = 8$, 1.6%).

Data concerning participants' responses with regard to reasons for tablet splitting and splitting difficulties are summarized in Table 3. The most common reason for tablet splitting was physician's order (41.2%) followed by unavailability of the prescribed dose (41.0%). About 30% of the participants experienced severe or moderate tablet splitting difficulties. About one quarter (24.0%) of study participants

Table 1 Demographic details of participants ($N = 491$)

Variable	n (%)
Age	
Mean \pm SD (57.2 years \pm 14.5)	
Median (57.0 years)	
Range (18–96) years	
Missing	4 (0.8)
Gender	
Female	265 (54.0)
Male	222 (45.2)
Missing	4 (0.8)
Educational status	
No schooling	57 (11.6)
Primary	67 (13.6)
Secondary	88 (17.9)
Community college	90 (18.3)
University	160 (32.6)
Higher education	21 (4.3)
Missing	8 (1.6)

sometimes skipped their doses due to tablet splitting difficulties.

Table 4 states participants' tablet splitting techniques and related issues. The majority of participants (63.5%) used

their hands to split tablets. In the case where tablet splitting resulted in two unequal parts, 16.4% of the participants ($n = 81$) stated that they waste parts of their medications or buy new medications from different sources with the exact dose.

Association analysis using the Pearson Chi-Square test for categorical variables studied the association between gender, age, educational status, most commonly split medications, reasons for tablet splitting, splitting techniques and tablet splitting difficulties. The results of the univariate analysis showed significant associations between gender, age, educational status, most commonly split medications and reasons for tablet splitting (P value <0.05). Significant associations were found between educational status, most commonly split medications, tablet splitting techniques and splitting difficulties (P value <0.05). Table 5 presents Pearson's Chi-Square analysis for the factors affecting the reasons for tablet splitting, tablet splitting techniques and tablet splitting difficulties.

Figures 1 and 2 represent reasons for tablet splitting and tablet splitting techniques among the different educational categories. Participants with college or university education split tablets most commonly based on physician's order (48.7%). However, participants who are illiterate or had school education only split tablets most commonly due to

Table 2 Most commonly split medications by participants ($N = 491$)

Brand name	Active ingredient	Manufacturer	Strength	Dosage form	Scored	n (%)
Salisal plus [®]	Aspirin	The United Pharmaceutical Manufacturing Co. Ltd., Jordan	325 mg	Caplet	No	187 (38.1)
Orfarin [®]	Warfarin	Orion Corporation, Finland	5 mg	Tablet	Yes	16 (3.3)
Euthyrox [®]	Levothyroxine	Merck KGaA, Germany	50 mcg	Tablet	Yes	14 (2.9)
Euthyrox [®]	Levothyroxine	Merck KGaA, Germany	100 mcg	Tablet	Yes	13 (2.6)
Blopress [®]	Candesartan	The Arab Pharmaceutical Manufacturing Co. Ltd., Jordan	16 mg	Tablet	Yes	11 (2.2)
Carvidol [®]	Carvedilol	Pharma International Co., Jordan	25 mg	Tablet	No	10 (2.0)
Atorvast [®]	Atorvastatin	Jordan Sweden Medical and Sterilization Co., Jordan	40 mg	Caplet	Yes	9 (1.8)
Lopressor [®]	Metoprolol	Novartis Pharma AG, Switzerland	100 mg	Caplet	Yes	9 (1.8)
Betaloc ZOK [®]	Metoprolol	AstraZeneca AB, Sweden	100 mg	Controlled release tablet	Yes	8 (1.6)
Concor [®]	Bisoprolol	Merck KGaA, Germany	10 mg	Film coated tablet	Yes	8 (1.6)
Diovan [®]	Valsartan	Novartis Pharma AG, Switzerland	160 mg	Film coated tablet	No	8 (1.6)
Hypoten [®]	Atenolol	HIKMA Pharmaceuticals, Jordan	100 mg	Tablet	Yes	7 (1.4)
Diostar [®]	Valsartan	Pharma International Co., Jordan	160 mg	Film coated tablet	No	6 (1.2)
Hypoten [®]	Atenolol	HIKMA Pharmaceuticals, Jordan	50 mg	Tablet	Yes	6 (1.2)
Lanoxin [®]	Digoxin	Aspen Bad Oldesloe GmbH, Germany	0.25 mg	Tablet	Yes	6 (1.2)
Lapril [®]	Enalapril	Middle East Pharmaceutical Co., Jordan	10 mg	Tablet	Yes	6 (1.2)
l-cor [®]	Bisoprolol	Jordan Sweden Medical and Sterilization Co., Jordan	5 mg	Film coated tablet	Yes	5 (1.0)
Esidrex [®]	Hydrochlorothiazide	Novartis Pharma AG, Switzerland	25 mg	Tablet	Yes	5 (1.0)
Glemax [®]	Glimepiride	Jordan Sweden Medical and Sterilization Co., Jordan	2 mg	Caplet	Yes	5 (1.0)
Prednisolone [®]	Prednisolone	The Arab Pharmaceutical Manufacturing Co. Ltd., Jordan	5 mg	Tablet	No	5 (1.0)
Revanin [®]	Paracetamol	The Arab Pharmaceutical Manufacturing Co. Ltd., Jordan	500 mg	Tablet	No	5 (1.0)
Sulpiren [®]	Sulpride	Medochemie Ltd, Cyprus	200 mg	Tablet	Yes	5 (1.0)
Others	–	–	–	–	–	135 (27.5)
Missing	–	–	–	–	–	2 (0.4)

Table 3 Participants' responses with regard to reasons for tablet splitting and splitting difficulties (*N* = 491)

Variable	<i>n</i> (%)
Reasons for tablet splitting*	
Physician's order	203 (41.2)
Unavailability of the prescribed dose	202 (40.9)
To decrease the dose	74 (15.1)
Swallowing difficulties	10 (2.0)
Saving money	2 (0.4)
Others	1 (0.2)
Missing	1 (0.2)
Patients experiencing tablet splitting difficulties [†]	
Never	218 (44.4)
Mild	123 (25.1)
Moderate	99 (20.2)
Severe	44 (9.0)
Missing	7 (1.4)
Patients skipping doses due to tablet splitting difficulties	
Always	2 (0.4)
Often	35 (7.1)
Sometimes	118 (24.0)
Rarely	159 (32.4)
Never	155 (31.6)
Missing	22 (4.5)

*More than one choice can be checked.
[†]As perceived by participants.

unavailability of the dose (63.2% and 59.4%, respectively). Participants from different educational levels most frequently chose to split tablets by hand. However, participants with college or university education showed the lowest percent frequency among other levels: 56.5% compared to 77.2% in the illiterate level and 72.3% in the school education level. Conversely, the percentage of participants splitting tablets by kitchen knife is the highest among participants with college or university education (19.2%).

Discussion

To the best of the authors' knowledge, this was the first study to investigate the practice of tablet splitting and the frequency of using different techniques for tablet splitting at outpatient pharmacies in Jordan. In Germany, 580 patients completed a questionnaire that evaluated the reasons for tablet splitting.^[11] The results showed that 94.1% of patients split tablets based on their prescription instructions and 5.6% of patients split tablets due to swallowing difficulties while 17 patients split tablets for other reasons with 10 patients stating that they split tablets to reduce the cost. The results of the previous study was in agreement with the results of the current study where the most common reason for tablet splitting was physician's order and to a lesser extent swallowing difficulties and cost reduction. However, other reasons, such as unavailability of the prescribed dose were not mentioned in the German study.^[11]

Medications that are Food and Drug Administration (FDA) approved for splitting have this information printed

Table 4 Participants' tablet splitting techniques and related issues (*N* = 491)

Variable	<i>n</i> (%)
Techniques used by patients to split tablets	
Hand broken	312 (63.5)
Kitchen knife	70 (14.3)
Tablet splitter	44 (9.0)
Teeth	29 (5.9)
Scissors	11 (2.2)
Combination of two or more of the above techniques	22 (4.5)
Others	1 (0.2)
Missing	2 (0.4)
Patients' responses with regards to their action when tablet splitting results in uneven two parts	
Disregard the difference and use either part	236 (48.1)
Tablet splitting always results in an even two parts	150 (30.5)
They use the larger part and discard the other	46 (9.4)
They use the smaller part and discard the other	15 (3.0)
Discard both parts and split a new tablet	9 (1.8)
Buy the medication from different source with the exact dose	11 (2.2)
Others	18 (3.7)
Combination of two or more of the above responses	6 (1.2)
Patients' responses with regards to their action when tablet splitting results in more than two parts	
Tablet splitting always results in two parts	234 (47.7)
Discard all parts and split a new tablet	138 (28.1)
I collect parts that equals a half-tablet and ingest them	67 (13.6)
Buy the medication from different source with the exact dose	12 (2.4)
Others	28 (5.7)
Combination of two or more of the above responses	12 (2.4)

in the package insert. In addition, tablets that are FDA approved for splitting are scored to facilitate the splitting. In the cases where the information about tablet splitting is not available in the package insert, the FDA cannot ensure weight and content uniformity of half-tablets. Moreover, the

Table 5 Pearson's Chi-Square analysis for factors affecting reasons for tablet splitting, tablet splitting techniques and tablet splitting difficulties

Variable	<i>P</i> value
Reasons for tablet splitting	
Gender	0.012
Age	0.029
Educational status	0.000
Most commonly split medications	0.000
Tablet splitting techniques	
Gender	0.279
Age	0.581
Educational status	0.004
Most commonly split medications	0.000
Splitting difficulties	
Gender	0.151
Age	0.239
Educational status	0.023
Most commonly split medications	0.001

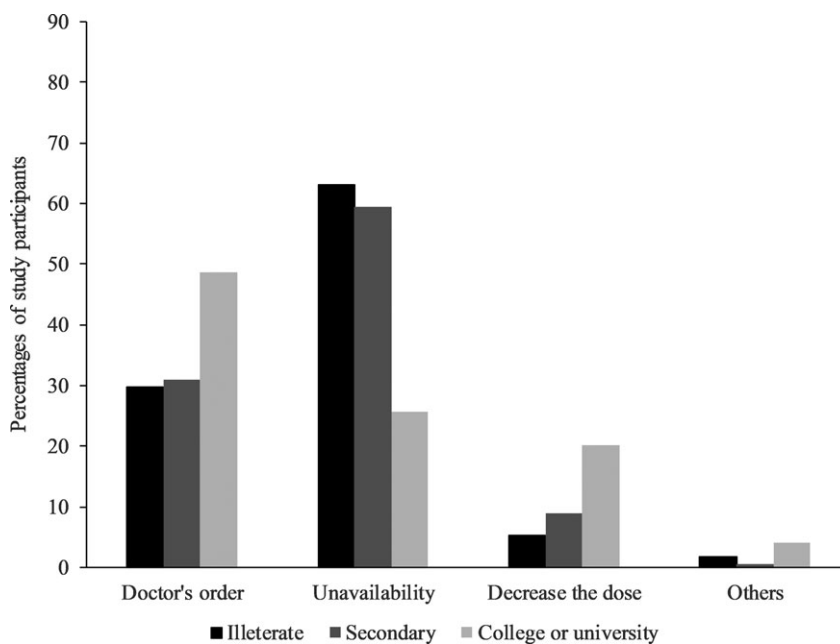


Figure 1 Reasons for tablet splitting among the different educational categories.

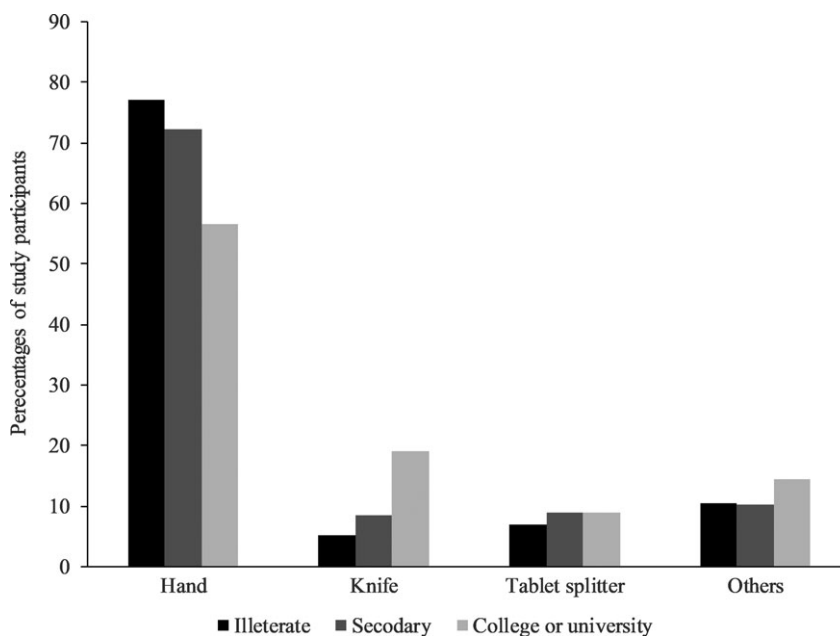


Figure 2 Tablet splitting techniques among the different educational categories.

FDA recommends splitting tablets just before ingestion because heat, humidity and other environmental factors can affect them.^[12]

Helmy^[13] recommended specific patient and drug criteria for tablet splitting as an appropriate practice. For example, long half-life, large size, flat and broad therapeutic index medications can be suitable for tablet splitting. However, narrow therapeutic index, small size, enteric coated and

extended-release medications are not suitable for tablet splitting.^[13]

With regard to splitting scored tablets, the results of the current study reported splitting scored controlled release or film coated tablets. However, the presence of a score-line can be misleading indicating that tablet splitting is allowed to obtain two equal doses. In Switzerland, a sample of nurses were asked if it is a correct practice to split all tablets with a

score-line. Sixty nine percent of the participating nurses agreed that splitting scored tablets is a correct practice.^[14] According to the package insert of the controlled release formulation metoprolol 100 mg (Betacloc ZOK[®] 100 mg) and the film coated valsartan 160 mg (Diovan[®] 160 mg), the score-line is to facilitate breaking the medication to overcome swallowing difficulty and not to produce two equal doses.^[15,16] Interestingly, 75% of participants who split Betacloc ZOK[®] 100 mg and Diovan[®] 160 mg split the mentioned medications based on physician's order. This raises the importance of activating the pharmacist's role in educating other healthcare providers with regard to which medication dosages can be split and which cannot. On the other hand, more than a tenth of the participants stated that they split tablets to decrease the dose not based on physicians' instructions but based on their own decision. This practice is risky and can compromise patients' health. The presence or absence of a score-line on a tablet can affect the weight variability and content uniformity of split tablets. FDA laboratories conducted a study to evaluate dose uniformity of two products: amlodipine and gabapentin.^[17] The results showed that splitting amlodipine tablets that lack a score-line resulted in content uniformity that is not accepted by USP criteria for content uniformity.^[17]

The results of the current study showed that about one quarter of the participants sometimes skipped their doses due to tablet splitting difficulties. This finding is alarming as medication non-adherence can decrease disease control and deteriorate patients' health outcomes.^[18,19] The majority of participants used their hands to split tablets. In addition, about one-third of the participants faced moderate or severe tablet splitting difficulties. Switching from one technique of tablet splitting to another can decrease splitting difficulties and accordingly can decrease medication non-adherence due to tablet splitting difficulties. Pharmacists have a vital role in detecting tablet splitting difficulties and concordantly design a plan with patients and other healthcare providers to overcome splitting difficulties either using different splitting technique or by eliminating the need for splitting. One of the major concerns of tablet splitting is drug waste. More than a tenth of the participants discarded parts or all of their tablets when the splitting did not result in equal parts. This puts an economic burden on both patients and the government, particularly since the two settings at which the current study took place were governmental. Strategies to avoid tablet splitting will decrease drug waste. For example, the Jordan Ministry of Health is implementing an electronic system to access medical records and process prescriptions, known as the Hakeem program.^[20] This system can be used to inform pharmacists and physicians about which medications can be split or not. It can also warn pharmacists about drug waste. Pharmacists and physicians are encouraged to work collaboratively to decrease tablet splitting which is expected to decrease drug waste.

Interestingly, the current study found an association between the educational level and reasons for tablet splitting and splitting techniques. Participants with a higher educational level most commonly split tablets based on physician's orders and less commonly due to unavailability or to decrease the dose. This indicates more awareness between participants with higher education about the importance of

following physician's orders and adhering to healthcare providers' recommendations.

Limitations of the study

Limitations may include recall bias in the participants' responses. Also, a pharmacist research assistant interviewed and administered the questionnaire which may have affected participants' responses. However, the use of a mailing or emailing system is not feasible or reliable in Jordan. This study was conducted in outpatient clinics in governmental hospitals in Irbid, the main city in the north of Jordan. Consequently, the results may not be generalizable to other private hospitals and other areas of the country.

Conclusion

The practice of tablet splitting resulted in drug waste and medication non-adherence. Drug waste is expected to increase the financial burden on both patients and the government. In addition, medication non-adherence can compromise a patient's health outcomes. Splitting controlled release and film coated preparations raises a major concern. Pharmacists are highly encouraged to educate healthcare providers and patients as to when tablet splitting is an acceptable practice.

Declarations

Conflicts of interest

The Author(s) declare(s) that they have no conflicts of interest to disclose.

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Authors' contributions

All Authors state that they had complete access to the study data that support the publication.

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