

Research Article
Open Access

Investigation of Information Printed on The Blister Pack of Loxoprofen Sodium Tablets

Yuuri Houchi^{1,2}, Hiroaki Tanaka¹, Kazunori Yamaguchi¹, Yuki Koshino¹, Hitoshi Houchi^{1,3*}, Minoru Miyake² and Shinji Kosaka¹

¹Department of Pharmacy, Kagawa University Hospital, Kagawa 761-0793, Japan

²Department of Oral and Maxillofacial Surgery, Faculty of Medicine, Kagawa University, Kagawa 761-0793, Japan

³Department of Clinical Pharmacy, Kagawa School of Pharmaceutical Sciences, Tokushima Bunri University, Kagawa 769-2193, Japan

ABSTRACT

Introduction: Loxoprofen sodium was selected as a commonly used medicine. The loxoprofen sodium tablets are marketed by 22 companies in Japan. The 22 different packaging types for this single active ingredient are served. We investigated the specifications printed on the 10-tablet blister pack.

Methods: Regarding specifications printing, using the 22 loxoprofen sodium products, the survey items included how many times each of the specific printing was printed on the 10-tablet blister pack. About the questionnaire survey, a question I assessed the desired number of specifications. Question II assessed the direct printing of the drug name on each of the tablets and the size of tablet. The target population of the survey consisted of prescribing doctors, nurses, pharmacists, and non-healthcare workers.

Result: The number of instances in which the drug name was listed ranged from 3 to 22 on the 10-tablet blister pack. The tablet identification code was printed ranged 0 - 10. Eleven products had no medical effect information on the pack. The expiration date was printed on two products. The serial number was not printed on one product.

On the questionnaire survey, the desired number of instances that the standard dose was printed was significantly higher for nurses and pharmacists than for prescribing doctors and non-healthcare workers. Nurses considered information about medical effects to be important. Pharmacists demanded more barcodes. Several identification codes were requested by health care professionals. Although many of the tablets were 9 mm in size, the respondents desired smaller tablets.

Conclusion: There were gaps between the amount of information printed on the pack and that was considered desirable by healthcare professionals and non-healthcare workers. Our findings indicate that multiple items are considered useful for developing packages for oral drugs marketed in the future as well as in ensuring safe and secure pharmacological therapy.

*Corresponding author

Hitoshi Houchi, Department of Clinical Pharmacy, Kagawa School of Pharmaceutical Sciences, Tokushima Bunri University, Kagawa 769-2193, Japan. Tel: +81 87 899 7427.

Received: January 20, 2023; **Accepted:** January 26, 2023; **Published:** February 01, 2023

Introduction

Many reported medical errors and incidents are related to pharmaceutical products [1-3]. Pharmaceutical products come in various dosage forms including infusions, injections, powders, tablets, and patches. The factors associated with errors and incidents differ by dosage form. Thus, discussing all dosage forms uniformly is impracticable.

Our present study focused on an oral drug commonly self-managed medication. Many tablets are marketed in blister packs. Handling errors by health care professionals and medication errors by patients can occur depending on the level of understanding of the information on the package. Based on this background, this

study selected loxoprofen sodium, which is prescribed by many clinical departments and which has many generic equivalents [4,5]. The efficacy of the branded and generic formulations was reported previously [4,6,7].

As of April 2021, loxoprofen sodium tablets (60 mg) are marketed by 22 companies in Japan, including the brand-name drug used in this study. Thus, there are 22 different packaging types for this single active ingredient, providing useful indices for investigating the demands of healthcare professionals and non-healthcare workers. Each box of loxoprofen sodium contains 10 blister packs of 10 tablets per pack. When seen by healthcare professionals and non-healthcare workers, the drug is commonly handled in

a 10-tablet blister pack rather than a box. Thus, the information printed on the 10-tablet blister pack is likely to contribute to safe and secure drug therapy. Under this background, we examined the information printed on the blister packs of all loxoprofen sodium tablet products available in Japan to identify the information considered important by health care professionals and non-healthcare workers.

Methods

Materials Expiration Date

Each box of loxoprofen sodium contains 10 blister packs of 10 tablets per pack. The expiration date is stated on the box. For 22 items, those with expiration dates longer than December 2022 were used.

Specifications Printing

Using the loxoprofen sodium products of 22 companies, the survey items included how many times each of the following specifications were printed on the 10-tablet blister pack: drug name, standard dose, company name (logo), medical effect, expiration date, serial number, method of removing the tablet from the pack, barcode, tablet identification code, and plastic mark. Other surveyed items included the color, printing form, size, and weight of the tablet. The tablet was pale red in color in all instances, and thus, the tablet color was removed as a survey item. Because the tablet size and weight are related, only the size was surveyed by the questionnaire. In addition, the tablets were 7, 8, 9, or 9.1 mm in diameter. For simplicity, 9.1 mm was considered 9 mm in the survey. Much of the aforementioned data were obtained from the drug package inserts.

Questionnaire Survey

The questionnaire survey was conducted from April 2021 to October 2022. The 10-tablet blister pack of loxoprofen sodium tablets has an area of approximately 32 cm² on one side. The question I assessed the desired number of specifications including the drug name, standard dose, company name, medical effect, date of production serial number, method of removing the tablet from the pack, barcode, tablet identification code, and plastic mark. Respondents chose from 4 categories for request number of 0, 1, 5, or 10 on each item. Question II assessed direct printing of the drug name on each tablet. Moreover, it was asked whether the appropriate tablet size was 7, 8, or 9 mm. The questionnaire survey

was conducted using full-scale images. The target population of this survey consisted of healthcare professionals and non-healthcare workers of Kagawa University Hospital and affiliated medical institution. In this survey, non-healthcare workers are people other than prescribing doctors, nurses, and pharmacists. The target population of the survey consisted of prescribing doctors (n = 59; 41 male and 18 female), nurses (n = 46; 0 male and 46 female), pharmacists (n = 48; 17 male and 31 female), and non-healthcare workers (n = 60; 23 male and 37 female). The age group of target population were classified to 20s, 30s, 40s, 50s, 60s and over 70. The 59 prescribing doctors were 37 physicians and 22 dentists. The prescribing doctors were 8 in their 20s, 15 in 30s, 19 in 40s, 12 in 50s, 4 in 60s, 1 in over 70. The nurses were 12 in their 20s, 13 in 30s, 12 in 40s, 8 in 50s, 1 in 60s. The pharmacists were 5 in their 20s, 16 in 30s, 15 in 40s, 8 in 50s, 4 in 60s. The non-healthcare workers were 12 in their 20s, 7 in 30s, 11 in 40s, 11 in 50s, 10 in 60s, 9 in over 70.

Ethics Statement and Statistical Analysis

This study was approved by the Ethics Committee of Kagawa Pharmaceutical Association (2020KAYAKU001). We used SPSS Statistics 24.0 (SPSS Inc., Chicago, IL, USA) for statistical analyses. The differences between the groups were compared using Tukey’s test. Statistical significance was set at P < 0.05.

Results

Table 1 summarizes the 22 loxoprofen sodium formulations available as prescription drugs in Japan. The number of times the drug name varied significantly from 3 to 22 times (mean, 14.8 ± 1.3). The mean number of times the standard dose (60 mg) was printed was 16.4 ± 1.2. The number of times the company name and tablet identification code were presented ranged from 0 - 8, which appeared to largely reflect the perspective of each company. Half of the products (n = 11) had no medical effect information on the pack. The expiration date was printed on two products. The serial number was not printed on one product. All products had information about the method of removing the tablet from the pack (mean, 1.8 ± 0.2), a barcode (mean, 1.6 ± 0.2), and a plastic mark (mean, 2.0 ± 0.3). One of two products featured direct printing of the drug name on the tablet. The mean tablet diameter, thickness, and weight were 8.6 ± 0.1 mm, 3.3 ± 0.1 mm, and 230.3 ± 9.2 mg, respectively.

Table 1: Information printing on the blister pack of loxoprofen sodium tablets (60mg) and each tablet

Product	Number of										Tablet		
	Drug name	Standard dose	Company name (logo)	Medical effect	Expiration date	Serial number	Taking method	Bar code	Identification code	Plastic mark	Print format	Size (mm)	Weight (mg)
A	21	21	2	3	0	1	1	1	3	1	E	9.1	250
B	11	10	0	0	0	0	2	1	0	2	E	8.0	170
C	11	10	0	5	0	1	1	4	0	1	NP	8.0	200
D	16	10	5	0	0	1	2	1	0	2	NP	8.0	200
E	10	9	0	4	0	1	4	1	10	4	E	9.1	240
F	22	22	0	4	0	1	1	1	5	1	E	9.0	300
G	3	23	0	0	0	1	2	1	5	2	E	9.0	250
H	20	15	0	0	0	1	1	1	8	1	E	9.1	250
I	12	12	5	2	0	1	1	2	10	1	E	9.0	250
J	11	6	0	5	0	1	2	2	5	3	E	9.1	275
K	20	20	0	0	0	1	2	1	0	2	E	8.0	201

L	21	21	1	1	0	1	1	1	1	1	E	9.0	250
M	11	16	2	0	1	1	1	1	10	1	E	9.0	250
N	19	17	0	3	1	1	1	2	10	1	E	9.0	250
O	14	16	0	3	0	1	2	1	0	3	E	8.0	180
P	11	16	8	0	0	1	4	1	7	4	E	7.0	130
Q	21	30	0	0	0	1	1	5	10	1	E	8.0	180
R	21	21	3	0	0	1	1	2	2	1	E	8.0	190
S	21	21	0	2	0	1	2	1	5	1	E	9.0	250
T	6	12	0	0	0	1	3	1	4	3	E	9.0	300
U	20	20	0	4	0	1	1	1	5	1	E	9.0	250
V	3	12	0	0	0	1	1	2	7	3	E	9.0	250

E : Engraved
NP : Name Print

In this questionnaire survey, the number of times each specification should be printed on the package (0, 1, 5, or 10) according to prescribing doctors, nurses, pharmacists, and non-healthcare workers was assessed. Figures 1 and 2 summarize the numbers of instances considered appropriate by respondents for each item. Figure 1 presents the mean number of instances considered appropriate for the drug name, standard dose, company name, medical effect, and expiration date. All groups desired for the drug name to be presented several times on the 10-tablet blister pack (7.8 ± 0.2), especially nurses (8.7 ± 0.4). In addition, nurses and pharmacists wanted the standard dose printed on the pack more times than did physicians and non-healthcare workers. Concerning company name, all groups did not request for to be frequently printed (1.7 ± 0.2), particularly nurses (0.6 ± 0.2). Conversely, nurses wanted the medical effects printed more times (4.7 ± 0.5) than did prescribe doctors, pharmacists, and non-healthcare workers (2.8 ± 0.2). The desired number of times the expiration date was printed was similar among the groups (1.9 ± 0.2).

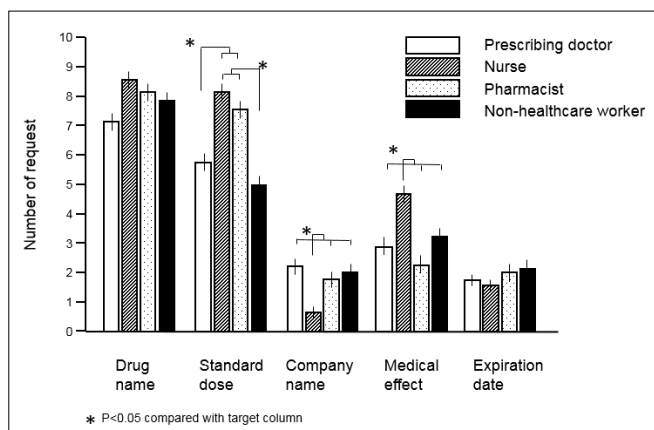


Figure 1: Mean number of instances on the blister pack requested by respondents (Part 1)

Figure 2 presents the mean numbers of instances considered appropriate for the serial number, method of removing the tablet from the pack, barcode, tablet identification code, and plastic mark. Concerning the serial number, the overall demand was low (1.0 ± 0.1). The desired number of times the method for removing the

tablet should be printed was significantly higher for nurses (3.5 ± 0.5) than for prescribing doctors, pharmacists, and non-healthcare workers (2.3 ± 0.2). Concerning the barcode, a higher number of instances was requested by pharmacists (4.1 ± 0.5) than by prescribing doctors, nurses, and non-healthcare workers (1.6 ± 0.2). Regarding the tablet identification code, prescribing doctors, nurses, and pharmacists wanted a high number of instances, whereas the desired number was low for non-healthcare workers (1.5 ± 0.3). All groups desired a low number of instances of plastic mark printing (1.4 ± 0.1) with no significant between-group difference. Subsequently, we investigated the need for direct printing of the drug name on the tablet. Overall, more than 85% of respondents deemed it necessary (prescribing doctors 78%; nurses 95%; pharmacists 97%; and non-healthcare workers 86%).

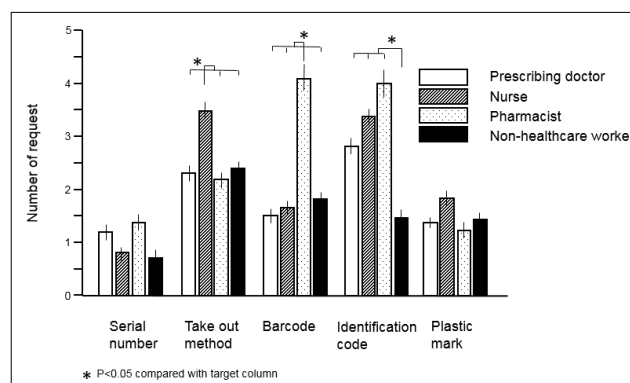


Figure 2: Mean number of instances on the blister pack requested by respondents (Part 2)

Figure 3 presents the desired size of the tablet (in diameter). As presented in Table 1, the size of marketed loxoprofen sodium tablets was 7, 8, and 9 mm for 1, 7, and 14 products, respectively. Figure 3 illustrates that the desired diameter was 7 mm for 64.6% of respondents (prescribing doctors, 64.8%; nurses, 61.5%; pharmacists, 52.6%; and non-healthcare workers, 79.6%) and 8 mm for 32.6% of respondents (prescribing doctors 31.5%; nurses 33.3%; pharmacists 47.4%; and non-healthcare workers 18.4%). A diameter of 9 mm was considered desirable by only 2.3% of respondents.

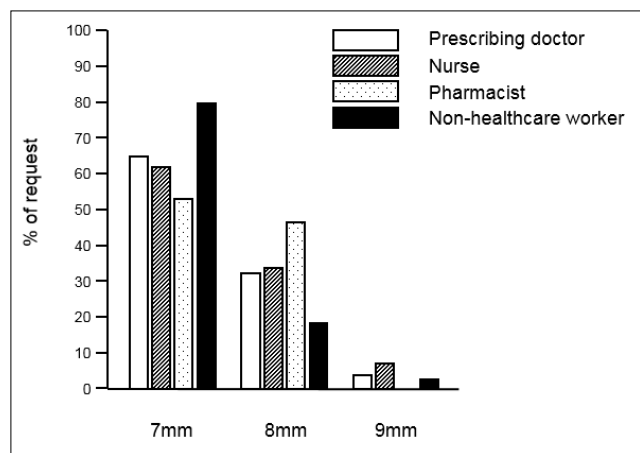


Figure 3: The desired tablet size of respondents

Discussion

This research investigated the perception of drug information among healthcare professionals and non-healthcare workers to help prevent medical malpractice. We focused on the level of understanding of the information printed on the tablet blister pack of an oral drug. Loxoprofen sodium is one of the drugs most generally prescribed in medical and dental treatments [8]. Loxoprofen sodium tablets (60 mg), including brand-name and generic formulations, are marketed by 22 companies, providing useful indices for investigating the demands of healthcare professionals and non-healthcare workers.

Table 1 summarizes the information printed on the blister pack and tablets for each product. The information on all products is printed in accordance with the law on securing the quality, efficacy, and safety of pharmaceuticals, medical devices, regenerative and cellular therapy products, gene therapy products, and cosmetics [9,10]. Although all products follow the law in Japan, the number of times each item is printed on the blister pack differed among the manufacturers. In particular, the number of times the drug name was printed on the pack greatly varied (3 - 22) on both sides of the pack, respondents of all job types considered it important information. In addition, the desired number of mentions of the drug name by all responders was also high, averaging 7.8 ± 0.2 times per side (Figure 1). The results indicated that the number of times the drug name is printed on the pack is the most important variable for healthcare professionals in promoting medical safety [11-13]. To prevent accidental ingestion, in addition to avoiding separating tablets unnecessarily when preparing and dispensing drugs, it may be necessary that the drug name can be identified even if tablets are separated by patients. The number of times the standard dose was printed also varied from 6 to 30 on both sides of the blister pack (Table 1). As presented in Figure 1, nurses and pharmacists wanted the standard dose printed more times than physicians and non-healthcare workers. The number of times the identification code was printed on the blister pack ranged from 0 - 10 (Table 1). The identification code is necessary to identify the drug name [14-16]. The desired number of instances was greater for nurses and pharmacists, who are often engaged in identifying drugs brought into a hospital by patients. By contrast, non-healthcare workers wanted the identification code printed 1.5 ± 0.3 times, suggestive of low interest (Figure 2). Whereas only 2 of 22 products (9%) had the expiration date printed on the blister pack (Table 1), approximately at least half of respondents considered it important. In particular, 88% of non-healthcare workers considered the expiration date important, suggesting

that it was regarded as equivalent to food labeling [17-19]. Thus, given the current percentage of products on which the expiration date is printed, the number of times the date is printed is a major issue to be addressed in the future. It is important that healthcare professionals, especially pharmacists, provide information to patients regarding residual medicine. For the medical effect, half of the products (11 products) had no information printed on the 10-tablet blister pack (Table 1). However, respondents considered this information important for inclusion in the pack. Concerning the details, pharmacists considered medical effect information less important than prescribing doctors, nurses, and non-healthcare workers. Because pharmacists are experts in medicine, they may know about the medical effects of drugs as a matter of course. Although healthcare workers may desire the medical effects to be printed on the tablet blister pack, considering that the drug studied in this research was the anti-inflammatory analgesic loxoprofen sodium, it is questionable whether similar results would be obtained if anti-cancer or psychotropic drugs were studied, and this must be an important consideration in the future. The mean number of times the barcode was printed on the blister pack was 1.6 ± 0.2 (Table 1). A barcode contains information including the drug name and standard dose in Japan [20]. The number of times the barcode was printed was considered an important item by pharmacists (4.1 ± 0.5 , Figure 2). Pharmacists identify the medicines brought into the pharmacy by patients or returned from wards. Scanning the barcode using a barcode reader to obtain various information might help to simplify operations. Although pharmacists understand the importance of barcodes, they may not have been selected because barcode readers are not widely used in Japan.

The drug name was directly printed on each tablet for two products (Table 1). Although not discussed in this report, direct printing of the drug name on each tablet was demanded by respondents in all groups, including 77.8% of prescribing doctors, 94.9% of nurses, 97.4% of pharmacists, and 85.7% of non-healthcare workers. Improved printing technology is essential for the direct printing of the drug name on each tablet [21,22]. Generic formations of loxoprofen sodium tablets have been on the market for some time because it is a general medicine. The printing technology has been improved during the process of marketing. Thus, it is likely that direct printing will become mainstream for future generic products. As presented in Table 1, the tablet was 9 or 9.1 mm in diameter in 14 of 22 products. The diameter was 7 mm for only one product. One probable reason for the predominance of the 9- or 9.1-mm diameter was that generic drug manufacturers designed their products to be 9 mm based on the 9.1 mm size of the brand-name drug. However, all groups desired 7 mm tablets (Figure 3), including 79.6% of non-healthcare workers. The respondents believe that the tablet size is important information to be provided on the drug pack. Because polypharmacy is a current issue [23-25], the preference for a smaller tablet size may have represented a feeling that medication needed to be minimized.

Conclusions

The purpose of our research was to help reduce medical errors of manufacturers. We focused on the level of understanding of the information printed on the tablet blister pack of oral drugs. Loxoprofen sodium was selected as a commonly used medicine.

For some items, there were gaps between the actual number of times the information was printed on the pack and that was considered desirable by healthcare professionals and non-healthcare workers. This could potentially cause medical malpractice and reduce

medication adherence. Our findings indicate that multiple items are considered useful for developing packages for oral drugs marketed in the future as well as in ensuring safe and secure pharmacological therapy. Also, the information in pack of medicines is important to avoid counterfeit drugs in markets.

Acknowledgements

We thank all staff at Kagawa University Hospital and affiliated hospitals and clinics who were involved in this study.

Funding

This research did not receive any specific grant from funding agencies in the public, commercial, or not-for-profit sectors.

Availability of data materials

All data supporting the conclusions are included in the article.

Declarations

Ethics approval and consent to participate

This study was reviewed and approved by the Ethics Committee of Kagawa Pharmaceutical Association (2020KAYAKU001).

Competing interests

The authors declare that have no competing interests.

References

1. Wastesson W J, Morin L, Tan C K E (2018) An update on the clinical consequences of polypharmacy in older adults: a narrative review. *Johnell K, Expert Opin Drug Saf* 17: 1185-1196.
2. Hoeve E C, Vries DE, Mol GMO, Sturkenboom CJMM, Staus MJMS (2021) Dissemination of Direct Healthcare Professional Communications on Medication Errors for Medicinal Products in the EU: An Explorative Study on Relevant Factors. *Drug Saf* 44: 73-82.
3. Linden-Lahti C, Takala A, Holmstrom AR, Airaksinen M (2021) What Severe Medication Errors Reported to Health Care Supervisory Authority Tell About Medication Safety? *J Patient Saf* 17: 1179-1185.
4. Greig L S, Garnock-Jones PK (2016) Loxoprofen: A Review in Pain and Inflammation. *Clin Drug Investig* 36: 771-781.
5. Nishimura F, Ushijima T, Nojima M, Hamada S, Hara K, et al. (2021) Comparison between the Effects of Loxoprofen and Acetaminophen on Postoperative Pain Following Radical Prostatectomy: A Propensity Score Matching Analysis. *Biol Pharm Bull* 44: 1427-1432.
6. Kim IW, Chung SJ, Shim CK (2002) Altered metabolism of orally administered loxoprofen in human subjects after an oral administration of loxoprofen for three consecutive days followed by a seven-day washout. *J Pharm Sci* 91: 973-979.
7. Komori K, Komae R, Yamazaki Y, Nakano S, Mitamura S, et al. (2013) HPLC-method for deliberation of drug mammary transfer-evaluation of over-the-counter drugs (Loxonin(®)-S, Bufferin(®) A) in mother mice *Yakugaku Zasshi* 133: 905-911.
8. Greig LS, Garmock-Jones PK (2016) Loxoprofen: A Review in Pain and Inflammation. *Clin Drug Investig* 36: 771-781.
9. Act on Securing Quality, Efficacy and Safety of Products Including Pharmaceuticals and Medical Devices <http://www.japaneselawtranslation.go.jp/en/laws/view/3213>
10. Pharmaceuticals and Medical Devices Agency., <https://www.pmda.go.jp/files/000218446.pdf>
11. Wittich MC, Burkle MC, Lanier LW (2014) Medication errors: an overview for clinicians. *Mayo Clin Proc* 89: 1116-1125.
12. Tseng HY, Wen CF, Jeng KC, Chen PL, (2018) Dispensing errors from look-alike drug trade names. *Eur Hosp Pharm* 25: 96-99.
13. Seoane-Vazquez E, Rodriguez-Monguio R, Alqahtani S, Schiff G (2017) Exploring the potential for using drug indications to prevent look-alike and sound-alike drug errors. *Expert Opin Drug Saf* 16: 1103-1109.
14. Raschke GC, Hatton CR, Weaver JS, Belgado S (2003) Evaluation of electronic databases used to identify solid oral dosage forms. *Am J Health Syst Pharm* 60: 1735-1740.
15. Ogawa K, Shiinoki Y, Kaneda T, Takane H, Shimada M (2016) Investigation of the Identification Codes Imprinted on Tablets, as well as of the Influence of These Codes on the Differentiation of Drugs Brought in by Patients, Which Have Been Dispensed as One-Dose Packages. *Jpn J Drug Inform* 18: 123-130.
16. Schiff DG, Kim S, Seger CA, Bult J, Bates WD (2006) Ability of practitioners to identify solid oral dosage tablets. *Am J Health Syst Pharm* 63: 838-843.
17. Ministry of Agriculture, Forestry and Fisheries. https://www.maff.go.jp/j/jas/kaigi/pdf/guide_0502.pdf
18. Neff AR, Spiker M, Rice C, Schklair A, Greenberg S, et al. (2019) Misunderstood food date labels and reported food discards: A survey of U.S. consumer attitudes and behaviors. *Waste Manag* 86: 123-132.
19. Liegeard J, Manning L (2020) Use of intelligent applications to reduce household food waste. *Crit Rev Food Nutr* 60: 1048-1061.
20. Pharmaceutical and Medical Devices Agency. <https://www.pmda.go.jp/safety/info-services/medical-safety-info/0005.html>.
21. Prasad KL, Smyth H (2016) 3D Printing technologies for drug delivery: a review. *Drug dev Ind Pharm* 42: 1019-1031.
22. Ameerduzzafar, Alruwaili KN, Rizwanullah M, Bukhari AN, Amir M, et al. (2018) 3D Printing Technology in Design of Pharmaceutical Products. *Curr Pharm Des* 24: 5009-5018.
23. Hoel WR, Connolly GMR, Takahashi YP (2021) Polypharmacy Management in Older Patients. *Mayo Clin Proc* 96: 242-256.
24. Kim J, Parish LA (2017) Polypharmacy and Medication Management in Older Adults. *Nurs Clin North Am* 52: 457-468.
25. Nguyen KJ, Fouts MM, Kotabe ES, Lo E (2006) Polypharmacy as a risk factor for adverse drug reactions in geriatric nursing home residents. *Am J Geriatr Pharmacother* 4: 36-41.

Copyright: ©2023 Hitoshi Houchi, et al. This is an open-access article distributed under the terms of the Creative Commons Attribution License, which permits unrestricted use, distribution, and reproduction in any medium, provided the original author and source are credited.