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Evaluation of Quality Parameters of Light Sensitive Drugs Marketed in Nepal

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ABSTRACT

Background: Photosensitivity is the response of drug or drug product to the exposure of solar, UV and visible light in the solid, semisolid, or liquid state that leads to a physical or chemical change. Exposure to light is a concern with numerous medications due to the potential for photo degradation or other chemical reactions that affect drug stability.

Methods: Out of all the registered brands in Department of Drug Administration, 9 brands of Rabeprazole tablets, 5 brands of Promethazine tablets and 5 brands of methylcobalamin tablets were selected and were subjected for testing and analysis for various quality parameters as per pharmacopoeia. The labels of the collected medicine were analyzed. The obtained data were entered and analyzed in Microsoft office excel 2019.

Results: Eleven products did not comply with the existing regulatory requirement on labeling system of medicine as per Regulation of Standard of drugs. There was no uniformity in mentioning the self-life. Similarly, large variation was seen on price of same generic drugs. Information regarding storage conditions, direction for use and category of the drug were lacking in the label of some brands of medicines. Upon Laboratory analysis, two brands of promethazine tablets and three brands of Rabeprazole tablets were found substandard. Drug content of all the brands of Methylcobalamin was found to contain overage.

Conclusions: The result of this study indicates that substandard medicines are abundant in Nepalese market. There is weak regulation monitoring which have resulted in no uniformity in similar pharmaceutical products too. Hence, stringent regulatory monitoring is required to assessthe quality of pharmaceutical products in the Nepalese market.

Keywords: Light sensitive drugs; substandard drugs; quality of drugs

INTRODUCTION

Substandard drugs are the drugs that do not comply with the standard specification as per the related pharmacopoeia or with the specification of the manufacturer or the requirement of the drug regulatory authority. Exposure to light is a concern with numerous medications due to the potential for photodegradation or other chemical reactions that affect drug stability.[1,2] Product instability may lead to under medication due to lowering of active drug concentration in dosage form and also lead to the formation of toxic products.[3]

Rabeprazole, Promethazine and Methylcobalamin are the commonly used drugs for their respective purpose but are light-sensitive drugs.[4-7] So, exposure to light is a concern with these medications due to the potential for photodegradation or other chemical reactions that affect drug stability. The quality of some brands of these drugs may not meet basic quality standards due to their contact with light during manufacture, packaging or storage. This study is concerned with the evaluation of Labelling parameters and drug content that reflects the quality of Rabeprazole, Promethazine and Methylcobalamin tablets available in the Nepalese market.

METHODS

A Cross-sectional laboratory based descriptive study was adopted to find the information about quality of light-sensitive drugs available in Nepalese market. Prior to collection of samples, ethical approval was sought from Institutional review committee of Central institute of science and technology, CiST College (IRC-CiST). Out of all the 38 DDA registered brands of Rabeprazole tablets, 8 brands of Promethazine tablets and 10 brands of Methylcobalamin tablets available in Nepal, 9 brands of Rabeprazole tablets, 5 brands of Promethazine tablets and 5 brands of methylcobalamin tablets were selected

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based on 1.5√n sampling rule and were subjected for testing and analysis for various quality parameters. All the brands registered in DDA were selected by lottery method and were collected randomly from DDA registered Pharmacy retail shops of Kathmandu valley and collected samples were analyzed in CiST College using all the required instruments. Experiments were conducted by using the validated methods as per the pharmacopoeia. Analysis of Promethazine and rabeprazole tablets was conducted as per the monograph of Indian pharmacopoeia. As analytical procedure of methylcobalamin tablets is listed only in Japanese Pharmacopoeia so analysis of methylcobalamin tablets was performed as per JP. All the analysis was performed from the duly calibrated instruments.

The labels of the collected products were analyzed for their compliance as per schedule-5 of Drug Category Rules 2043 (1986).[8] The obtained data were entered and analyzed in Microsoft excel.

RESULTS

In this study, 19 brands of light-sensitive drugs were studied comprising 9 brands of rabeprazole, 5 brands of promethazine and 5 brands of methylcobalamin. Manufactured date of all the collected samples were within 6 months from manufactured date. It was found that 11 products did not comply with the existing regulatory requirement on labelling system of medicine as per schedule-5 of Drug Category Rules 2043 (1986).[8] Upon analyzing 18 points of labelling parameters mentioned in schedule 5 of Drug category rules, 2045 there is no uniformity in drug schedule categorization. All three drug products (Promethazine, Rabeprazole and Methylcobalamin tablets) should be dispensed under prescription of registered medical practitioner only. So, schedule 5 of Drug category rules, 2045, they should be categorized under Samuha Kha (Category "B" for Domestic Products) or Schedule H (Indian Products). In this study, five drugs (26.32%) were categorized under Samuha Ga and 2 drugs (10.53%) were not categorized.

While evaluating the pharmacopeial standard of the samples, it was found that 21% brands did not mention about the pharmacopeial standard they are following.

Table 1. Regulatory compliance on labeling.

Regulatory Parameters	Percentage (%) (n=19)
Manufacture date mentioned	100
Expiry date mentioned	100
Batch number mentioned	100
Direction for use	42.11
Caution mentioned	89.47
Storage condition	100
Samuha not mentioned	10.53
Wrong Samuha	26.32

There was no uniformity in mentioning the shelf-life. Variation in shelf life was seen among different brands of same generic drug product also. Table 1 illustrates the variation of shelf life. Similarly, variation was seen in price among different brands of same generic drugs as illustrated in table 2.

Table 2. Shelf-life (Expiry) duration.

Tablets	1 year	1.5 years	2 years	3 years
Promethazine	0	0	1	4
Rabeprazole	1	3	5	0
Methylcobalamin	0	0	5	0
Total	1	3	11	4
%	5.26	15.79	57.89	21.05

Table 3. Analysis of price of drugs.

Tablets	Max	Min	Mean	% Variation
Promethazine	6.72	2.60	4.46	92.29
Rabeprazole	12.00	10.00	11.27	17.75
Methylcobalamin	20.00	15.68	19.14	22.58

Among 19 total brands that were tested in laboratory of CiST College in this study, five brands (26.31%) were found to be substandard. Among the substandard drugs, two brands were of promethazine tablets and three brands were of Rabeprazole tablets. All the 5 brands of methylcobalamin were found to contain more drug content than pharmacopoeial limit. As per limit set by monograph in Pharmacopoeis, drug content must be within 90 - 110% whereas in case of water soluble vitamins, not more than 150% of the drug content is considered to be acceptable.[9] 4 brands of methylcobalamin were found to contain more overage than 150%. These brands may not be considered substandard but maximum of overage drug content may lead to side effects to the consumers.

Table 4. Drug Schedule, Packaging and Coating condition of Samples.

Tablets	Code	Drug Schedule	Light resistant Packaging	Coating

Promethazine	P1	Kha	Yes	Uncoated
	P2	Ga	Yes	Uncoated
	P3	Ga	No	Film
	P4	Kha	No	Film
	P5	Kha	Yes	Film
Rabeprazole	R1	Kha	Yes	Enteric
	R2	Kha	Yes	Enteric
	R3	NM	Yes	Enteric
	R4	Kha	Yes	Enteric
	R5	Ga	Yes	Enteric
	R6	Ga	Yes	Enteric
	R7	H	Yes	Enteric
	R8	H	Yes	Enteric
	R9	Kha	Yes	Enteric
Methylcobalamin	M1	Ga	Yes	Uncoated
	M2	Kha	Yes	Uncoated
	M3	NM	Yes	Film
	M4	Kha	Yes	Uncoated
	M5	Kha	Yes	Uncoated

Table 5. Quality parameter evaluation of Samples.

Tablets	Code	Weight variation	DT	Assay	Dis-solution	Content Uni-formity
Promethazine	P1	C	C	C	DNC	NA
	P2	DNC	C	C	DNC	NA
	P3	C	C	C	C	NA
	P4	C	C	C	C	NA
	P5	C	C	C	C	NA
Rabeprazole	R1	C	C	C	C	NA
	R2	C	C	C	C	NA
	R3	C	DNC	C	DNC	NA
	R4	C	C	C	C	NA
	R5	C	C	C	C	NA
	R6	C	C	DNC	DNC	NA
	R7	C	DNC	DNC	DNC	NA
	R8	C	C	C	C	NA
	R9	C	C	C	C	NA
Methylcobalamin	M1	C	C	C	NA	C
	M2	C	C	Overage	NA	C
	M3	C	C	Overage	NA	C
	M4	C	C	Overage	NA	C
	M5	C	C	Overage	NA	C

C: Complies, DNC: Does not comply, NM: Not mentioned, NA: Not Applicable, DT: Disintegration Test

DISCUSSION

It was found that 11 products did not comply with the existing regulatory requirement on labelling system of medicine as per schedule 5 of Drug category rules, 2045. Price Variation was observed ranging from 22.58% to 92.29%. A similar study was carried out in Kathmandu valley which had shown that out of 34 generics studied, 25 of them had more than 50% price variation.[10] Tablets containing light-sensitive drugs must be coated in order to protect degradation of the drug but among 19 brands, tablets of 6 brands (31.58%) were found to be uncoated. Although all of these drug products contain light resistant packaging, there still remains the risk of drug degradation during administration of drug.

Among 19 brands that were tested in laboratory of CiST College five brands (26.31%) were found to be substandard, as analysis results of their quality parameters were not as per limits of Pharmacopoeia. Among the substandard drugs, two brands were of promethazine tablets and three brands were of Rabeprazole tablets. All the five brands of methylcobalamin were found to contain overage. This data is lower than the result obtained in a similar study done by Gyanwali et al in Kathmandu valley which identified 32.5 % substandard medicines among 40 brands analyzed.[10]

This study indicates that, substandard medicines still exist in Nepalese market. Low income countries are particularly exposed to poor-quality medicines and sub-standard products.[11] According to Drug Bulletin of Nepal, out of 687 samples tested in National Medicine Laboratory, 14.4% samples were found substandard. But 41.9% (57 out of 136) samples failed to meet standard which were received from its branch offices and inspection division.[12]

CONCLUSIONS

The result of this study indicates that substandard medicines still exist in Nepalese market. This indicates there might be weak regulation monitoring which have resulted in no uniformity in similar pharmaceutical products too. The basic labelling requirements in some drug products were found not being adhered to the regulatory guidelines of Drug category rules, 2045 prepared by Department of Drug administration. The study has suggested that stringent regulatory monitoring is required to assess the quality of pharmaceutical products in the Nepalese market.

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CONFLICT OF INTEREST

The authors declare no conflict of interest

REFERENCES

1. Ahmad I, Ahmed S, Anwar Z, Sheraz MA, Sikorski M. Photostability and photostabilization of drugs and drug products. International Journal of Photoenergy. 2016;2016. doi:10.1155/2016/8135608
2. University of Illinois at Chicago College of Pharmacy DIG. Light-Sensitive Injectable Prescription Drugs. Hospital pharmacy. 2014;49(2):136-63. doi:10.1310/hpj4902-136
3. De Oliveira Melo SR, Homem-de-Mello M, Silveira D, Simeoni LA. Advice on degradation products in pharmaceuticals: a toxicological evaluation. PDA Journal of Pharmaceutical Science and Technology. 2014;68(3):221-38. doi:10.5731/pdajpst.2014.00974
4. Garcia CV, Nudelman NS, Steppe M, Schapoval EE. Structural elucidation of rabeprazole sodium photodegradation products. Journal of pharmaceutical and biomedical analysis. 2008;46(1):88-93. doi:10.1016/j.jpba.2007.09.002
5. PubChem. Methylcobalamin. In: Medicine NLo, editor.
6. Chamle A, Shane N, Pai A, Muddukrishna B. Photodegradation of methylcobalamin and its determination in a commercial formulation. Indian Journal of Pharmaceutical Sciences. 2019;81(1):57-62. doi:10.4172/pharmaceutical-sciences.1000479
7. Perkins S, Evans A, King A. Updated List of Light-Sensitive Oral Medications. Hospital pharmacy. 2020;55(6):349-65. doi:10.1177/0018578719844699
8. Drug Category Rules, 2043 (1986), (2043 (1986)).
9. Yoo SJ, Walfish SL, Atwater JB, Giancaspro G, Sarma N. Factors to consider in setting adequate overages of vitamins and minerals in dietary supplements. InPharm. Forum 2016 Jan (Vol. 42, pp. 111-114).[Download PDF]
10. Gyanwali P, Humagain B, Aryal K, Pandit A, Acharya T, Bista B, et al. Surveillance of quality of medicines available in the Nepalese market: a study from Kathmandu Valley. J Nepal Health Res Counc. 2015;13(31):233-40.[JNHRC]
11. Ravinetto RM. Poor-quality medicines: from knowledge to control and prevention. 2014.doi:10.1179/2047772414Z.000000000207
12. Drug Bulletin of Nepal (DBN). 2014 A.D.