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Original article

IN-VITRO EVALUATION OF DIFFERENT AVAILABLE BRANDS OF DEXLANSOPRAZOLE MR CAPSULES.

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Running Title: In-Vitro Evaluation of Different Available Brands of Dexlansoprazole MR Capsules

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Abstract

Dexlansoprazole delayed release is a newly developed class of Proton Pump Inhibitor (PPI). The drug is effective in the treatment of erosive esophagitis, maintenance of eosinophilic esophagitis and relief of heartburn. Additionally, it is also beneficial in the treatment of heartburn with symptomatic gastroesophageal reflux disease. The drug offers the advantage of no dosage adjustment in patients with hepatic impairment. Dexlansoprazole inhibits the stomach acid secretion by specific inhibition of the hydrogen-potassium-ATPase in parietal cells of stomach. Dexlansoprazole inhibits the final step of acid production. The purpose of this study was to perform in-vitro evaluation of different randomly selected brands of dexlansoprazole available in the market. The in-vitro evaluation was performed by assessing the quality control testing parameters i.e. weight variation, disintegration and dissolution test as specified in BP/USP. All the three brands were found to comply with the official pharmacopeial limits of weight variation, disintegration and dissolution. As the therapeutic response of a drug depends largely on its quality parameters, hence, it is concluded that the brands investigated in the study can be interchangeably used owing to their similar quality profile.

Introduction

Dexlansoprazole is a newly developed PPI. It is the (R)-enantiomer of lansoprazole Fig 1 [1]. It gives prolong elimination rate as compared to (S)-lansoprazole. Chemically, dexlansoprazole is (+)-2-[(R)-{[3-methyl-4-(2, 2,2trifluoroethoxy) pyridin-2-yl] methyl} sulfinyl]-1H-benzimidazole and it works by preventing acidic secretions of stomach. Molecular weight of dexlansoprazole is 369.36 while molecular formula is C₁₆H₁₄F₃N₃O₂S [2].

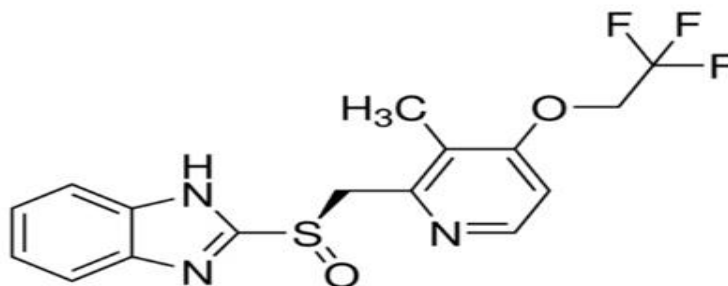


FIGURE1: Dexlansoprazole structure

Dexlansoprazole Modified Release (MR) is developed to deliver the medication in two phases [3]. Dexlansoprazole have been approved by FDA since January 2009[4], for the symptomatic relief of GERD and for the management of cured erosive esophagitis with approved dose of 30 and 60 mg to

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be given once daily [5]. The mode of action (MAO) of dexlansoprazole and other PPI is to prevent the activity of enzyme found in mucosa of stomach, the (H/K ATPase) known as the proton pump [6]. The enzyme hydrogen/potassium adenosine triphosphate secretes HCL, by hydrolyzing adenosine triphosphatase and interchange hydrogen with potassium ions which stimulate the acid secretion [7]. The dexlansoprazole MR capsules releases the active drug at PH 5.5 and 6.8, thereby, forming first peak at two hours and the other peak at 4-5 hours after drug administration. The drug also offers the advantage to be given without regard to meals [8]. Dexlansoprazole MR gives maximum dosing compliance. The duration of this drug as compared to PPI failure patients remains illuminated, as they manage their symptoms at once daily dose of dexlansoprazole [9]. Dexlansoprazole has a longer elimination half-life as compared to other proton pump inhibitors and it retains in the serum plasma for a long period of time [10]. The (AUC) area under the curve value is three to five times higher as compared to other racemic mixtures [11]. The metabolism of dexlansoprazole takes place in the liver by oxidation reduction process in the presence of CYP450 enzymes, and forms sulphonic metabolites [12]. Bioavailability of certain drugs depends on the pH of the gastric environment such as atazanavir and nelfinavir. Dexlansoprazole may interact with these drugs, for example, antifungals like ketoconazole and itraconazole. Their systemic absorption is dependent on low pH values so dexlansoprazole should be avoided when using these drugs [13]. The serious side effects of dexlansoprazole include increased risk of diarrhea. Long term use of the drug may lead to clostridium difficile infection in the intestine. The long-term and multiple daily dose of the drug is associated with an increased risk for osteoporosis-related fractures of the hip, wrist or spine, while, other common side effects are nausea, vomiting, headache, and constipation [14].

Material and Method

Study Design

In vitro comparative quality control parameters had been assessed of various commercially available brands of dexlansoprazole. The comparison was carried out by performing various quality control tests as specified by the official pharmacopeias i. e. weight variation, disintegration, and dissolution parameters. The brands were labelled as dug 01, 02 and 03 as specified in table 1.

Weight Variation Test

The in-process quality control parameter weight variation is performed to assure that each capsule dosage form is consistent during the process of compression. For current investigation, 10 capsules of each brand of dexlansoprazole were weighed on electronic Balance FX-400. Capsules were found to be passed if the weight lies within the limit specified by the United States pharmacopeia, i.e. 80 mg or less NMT, and not more than 2 deviate from average weight by 10% as shown in table 2.

Disintegration Test

Disintegration test determines whether the capsule will disintegrate within a specified time period when placed in a medium under the suitable conditions. The disintegration test was performed on the curro model number DS-0702 apparatus. Water was used as the dissolution medium where temperature was maintained at (35 °C to 39 °C). Each capsule was placed in each of the six tubes of the basket. The capsules were monitored until they completely disintegrated. The test requirements are met if not less than 16 of the 18 capsules are disintegrated. The disintegration limit for capsules according to BP/USP is not more than 30 minutes [15].

Dissolution Test

The in-vitro dissolution test is used as a qualitative tool to provide the measurement of bioavailability

of a drug as well as to demonstrate the bioequivalence from batch-to-batch. Galvano scientific GDT-7L dissolution apparatus was used for the current investigation. 900 ml of water was placed in each vessel with temperature maintained at $(37^{\circ}\text{C} \pm 0.5^{\circ}\text{C})$. The apparatus was operated at 50 RPM. Each capsule was placed in the vessel. Volume measuring 10 ml of solution was withdrawn at different time intervals i.e. at 15, 30, 45, and 60 minutes from each vessel. Absorbance of the sample was measured using UV spectrophotometer. Similar procedure was performed for the standard solution. Absorbance of sample solution was compared to that of the standard solution. As per the standard, capsules were found to comply the test if more than 85% of the drug is released in 30 minutes.

Statistical Analysis

All the data was analyzed using Microsoft Excel to evaluate its compliance with the pharmacopoeial standards.

TABLE 1: Specification of drugs

NO	Brand Name	Serial number	Batch number
1	Razodex	Drug-01	025C47
2	Dolgina	Drug-02	132255
3	Dexxoo	Drug-03	203

TABLE 2: Weight variation test limits

IP/BP	Limit	USP
80 mg or less	$\pm 10\%$	Less than 130mg
More than 80mg or Less than 250mg	$\pm 7.5\%$	130mg to 324mg
250mg or more	$\pm 5\%$	More than 324mg

TABLE 3: Weight variation of commercially available brands of Dexlansoparazole

Brand Name	Batch Number	Average weight (mg)	Standard deviation (mg)	Upper Limit (UCL) (X+3S)	Lower limit (LCL) (X -3S)
Razo(01)	025C47	1.796	1.553	2.2620	-0.3107
Dolgi(02)	132255	2.415	2.590	3.1920	-0.5180
Dexo(03)	203	1.784	3.169	1.8790	-0.0633

Average weight (x)mg U.S.P	Drug-01 weight(mg)	Drug-02 weight (mg)	Drug-03 weight (mg)
1	1.78	2.54	1.76
2	1.74	2.01	1.82
3	1.74	2.55	1.76
4	1.75	1.85	1.76
5	2.23	2.56	1.82
6	1.78	2.53	1.76
7	1.74	2.54	1.77
8	1.68	2.54	1.81
9	1.74	2.49	1.75
10	1.78	2.54	1.83

Table 4: Weight variation table

TABLE 5: Disintegration test and limits

Serial number	Batch No	Disintegration Test Time	Official Limit	Remarks
Drug-01	025C47	2.85	NMT 15min	Pass
Drug-02	132255	1.55	NMT 15min	Pass
Drug-03	203	1.3	NMT 15min	Pass

Result

Different commercially available brands of Dexlansoprazole 30 mg MR capsules namely Razodex, Dolgina and Dexxo had been evaluated in-vitro. Weight variation test revealed average weight of the three brands as 1.796, 2.415, and 1.784 mg with their Uper and lower control limits as 2.262 -0.310, 3.192 -0.518, 1.879 -0.063 mg as shown in Table, 3 & 4. Disintegration test revealed that

Razodex took more time to disintegrate as compare to Dolgina and Dexxoo as shown in Table 5. However, all the drugs disintegrated within the limits or specification as provided by USP i.e. less than 15 minutes.

All the brands of dexlansoprazole i.e. Razodex, Dolgina and Dexxoo capsules released more than 85% drug at 30 minutes, hence, comlying with the official limits as shown in table 6 and 7.

TABLE 6: Dissolution test and limits

S. No	Batch No	Dissolution Percentage	Official Limit	Remarks
Drug-01	025C47	86%	NLT 75%	Pass
Drug-02	132255	95%	NLT 75%	Pass
Drug-03	203	90%	NLT 75%	Pass

Table 7: Dissolution absorbance test

S.No	Batch No	Absorbance At 15 min	Absorbance At 30 min	Absorbance At 45 min	Absorbance At 60 min
Drug-01	025C47	2.139	0.761	0.664	0.468
Drug-02	132255	2.446	1.788	0.548	0.354
Drug-03	203	1.623	1.494	0.574	0.355

Discussion

Globally, a number of individuals suffer from GERD, which, if not treated could progress to a number of gastric complications. Despite numerous advancements, PPIs remain the main reserve in the management of GERD. However, a number of factors associated with PPIs tends to decrease their use in the management of GERD [16].

Dexlansoprazole is the seventh PPI to be introduced in the market. Unlike to its previous analogues, it offers the advantage of once daily dosing along with better tolerability. Moreover, it can be taken without regard to food.

The therapeutic effectiveness of a drug is closely correlated with its quality. The Organization for International Standards define quality as “the totality of features and characteristics of a product or service that bears its ability to satisfy stated or desired needs”. Not only effectiveness, safety is also guaranteed when the product is of superior quality [17-19].

The present study investigated the quality control parameters of various commercially available brands of dexlansoprazole namely Razodex, Dolgina & Dexxo. Weight variation, dissolution and disintegration are interlinked to each other and have a significant influence on absorption and bioavailability of the drug. For the current investigation, weight variation, dissolution and disintegration were employed as the quality control parameters. All the brands complied with the standard pharmacopeial limits and no difference was observed in the quality of these brands.

Conclusion

Dexlansoprazole is a new generation proton pump inhibitor, effective in the management of gastric reflux diseases. All the commercially available brands of dexlansoprazole were found to be within the official pharmacopeial limits. The therapeutic response of a drug depends largely on its quality parameters, hence, it is concluded that the brands investigated in the study can be interchangeably used owing to their similar quality profile.

Data Availability

No data have been adapted from any research or paper; all the data have been collected in the research lab while the standards were taken from the official guideline (USP/BP).

Conflicts of Interest

The authors declare that they have no conflicts of interest. All contributing authors are academicians and researchers.

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