

COMPARISON OF QUALITY CONTROL OF TWO DIFFERENT B-COMPLEX TABLETS AND THEIR LEGISLATIVE ISSUES ON THE ALBANIAN PHARMACEUTICAL MARKET

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Abstract

The aim of this study is to compare two different productions of Albanian and Canadian B-complex multivitamin tablets on the Albanian pharmaceutical market through various ‘in vitro’ pharmacopeias tests and argue about the regulatory legislative framework of drugstore sale of these products. Identification, weight uniformity, hardness and disintegration tests are carried out for the specific vitamins pyridoxine, niacin and riboflavin in these multivitamin B-complex tablets. The quality control tests implemented for the different productions of Albanian and Canadian B-complex tablets ensues that both of the productions fulfill the limits of pharmacopoeia for the presented tests. In the comparison of these products, it is noticed difference in technological formulation, packing and price per tablet. The retrospective analysis of the legislative framework shows a gap in the marketing and sale protection for these multivitamin tablets as genuine pharmaceutical products.

Keywords: Quality Control, Multivitamin Tablet, Pharmaceutical Market

Introduction

The aim of this study is to make a comparison of two different productions of B-complex multivitamin tablets, Canadian and Albanian, available in the Albanian Pharmaceutical market. The comparison is evaluated through different quality control tests and costs. It also argues about the regulatory legislative regulation of drugstore sale of these products. The comparison is evaluated through performing the quality control tests. Quality control is that part of the GMP that includes the taking of the samples, specifications and analysis, organization, documentation and release/admission procedures that guarantee that the respective and necessary

analysis are performed and that the materials are not admitted/released for usage, nor the products are not admitted/released for sale or supply until the moment that their quality must be considered as acceptable. Both productions of B-complex multivitamin tablets are registered in the Albanian Pharmaceutical market by the Registration Authorities and consist of common specific vitamins of Riboflavin (B2), Pyridoxine (B6) and Niacin (B3). Riboflavin is involved in the energy production for the electron transport chain, the citric acid cycle, as well as the catabolism of fatty acids (beta oxidation) . Pyridoxine is linked to cardiovascular health by decreasing the formation of homo cysteine. Pyridoxine may help balance hormonal changes in women and aid the immune system (Kashanian, M.; Mazinani, R.; Jalalmanesh, S., 2007). Niacin is the oldest lipid lowering drug. It reduces secondary outcomes associated with atherosclerosis, such as low density lipoprotein cholesterol (LDL), very low-density lipoprotein cholesterol (VLDL-C), and triglycerides (TG), but increases high density lipoprotein cholesterol (HDL) (Villines TC, Kim AS, Gore RS, Taylor AJ 2012).

The B-complex vitamin tablets are included in the nutritional supplement group and therefore are controlled by the Albanian Drug Authorities according to the operative legislation. Today, this legislation lacks in the inclusiveness of all multivitamins productions in the dietary/nutritional supplements regulations.

Materials and Methods

Reagents and chemical agents used in the study for the experimental part are two different productions of B komplex multivitamin tablets Canadian and Albanian productions. The main apparatus used are analytical scale, Varian hardness test apparatus, Varian UV-Vis Spectrophotometer, disintegration apparatus Guoming BJ-2. Subject to the quality control test are the common specific vitamins of Riboflavin (B2), Pyridoxine (B6) and Niacin (B3) that constitute the two different productions of B komplex multivitamin tablets.

Calibration Curves

For each vitamin (Riboflavin, Pyridoxine and Niacin) contained in the B komplex multivitamin tablets, the calibration curves are designed. For Riboflavin, mother water solution of 100 μ g/ml is created by dissolving 100mg riboflavin in 100ml NaOH 0,1N and 10ml of this solution is diluted in 100ml NaOH 0,1N. Therefore the calibration solutions are obtained (5-20 μ g/ml). NaOH 0,1N is used as blank.

For Pyridoxine the mother solution was obtained from dissolving 10 mg of pyridoxine in 100ml carbon dioxide-free water. This is 0,1 mg/ml

mother solution. The standard solutions are created in the concentrations 0,5-20 μ g/ml. Water was used as blank.

200 mg of Niacin are dissolved 500ml in carbon dioxide-free water. Mother solution 0,4 mg/ml was obtained. The standard solutions are 8-40 μ g/ml. Water was used as blank.

For every solution, the absorbance is measured in the maximum absorbance wavelength (respective λ_{\max} riboflavin=450nm; λ_{\max} pyridoxine=290.1nm; λ_{\max} niacin= 259.9nm). The calibration curves were carried out and designed through Cary Varian data software.

Identification

Identification of the presence of riboflavin in each production of B complex vitamin tablet was performed through spectrophotometric method. 1 tablet of each production was dissolved in 3ml NaOH and 3ml glacial acetic acid, and then diluted in 100ml H₂O. The spectrum was obtained in the spectral range [200-500nm]. The absorbance ratios were evaluated A273/A267, and A444/A264 according to European Pharmacopeia 5.0, in the monograph 'Riboflavin identification' (pg 2366).

Identification of Pyridoxine was performed by dissolving 2.50 g of pyridoxine in 50ml in carbon dioxide-free water (solution S). Solution S should give typical reaction of chlorides (2.3.1 EuPh 5.0) of deep red color.

Identification of Niacin was made by evaluating the ratio A237/A262 from the niacin spectrum of the solutions of 20 μ g/ml of each production according to the United States Pharmacopoeia National Formulary monograph, 'Niacin identification' (pg 1080-1081).

Weight Variation

20 tablets of each production of B-complex tablets were weighted individually. Then the average weight (g) was evaluated as well as standard deviation (stdev) and the percentage deviation. The statistical evaluations were performed with Microsoft Office Excel 2007.

According to USP limits of weight variation, not more than two of the individual weight can deviate from the average weight of not more than 10% according to The United States Pharmacopoeial Convention (2011), that discusses about Uniformity of Dosage Units.

Hardness test

Hardness test is a non pharmacopeia test. Oral tablets have a hardness of 4-10kg (Bettiol, 2010). 10 tablets of each production of B-complex tablets were measured individually. The average hardness and standard deviation (stdev) was evaluated through Microsoft Office Excel 2007.

Disintegration test

3 tablets of each production of B-complex tablets are measured for the disintegration test in distilled water (900ml, 37°C, 30 min) in Guoming BJ-2 apparatus. One dosage unit was placed in each of the six tubes of the basket. According to USP, if one or two dosage units fail to disintegrate, the test is repeated on 12 additional dosage units. The requirements of the test are met if not less than 16 of the 18 dosage units tested are disintegrated according to Revision Bulletin Official (2008).

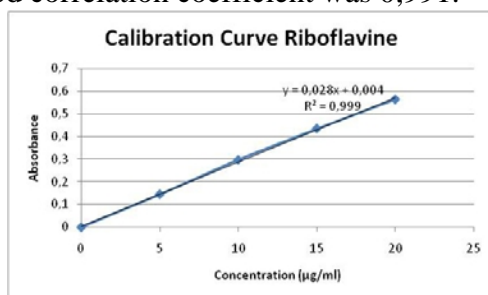
Legislative regulation

Legislative regulation for nutritional supplements in Albania was analyzed through the currently operative directive *Law Nr. 9323 date 25.11.2004 «Drugs and pharmaceutical service», regulation «Registration of drugs in the Republic of Albania».*

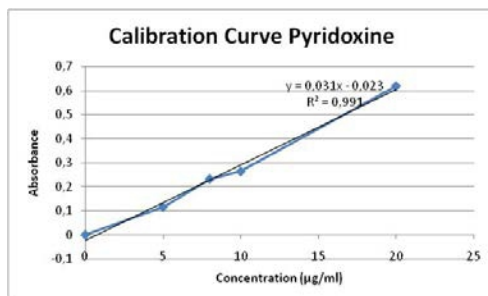
Results

Calibration Curve

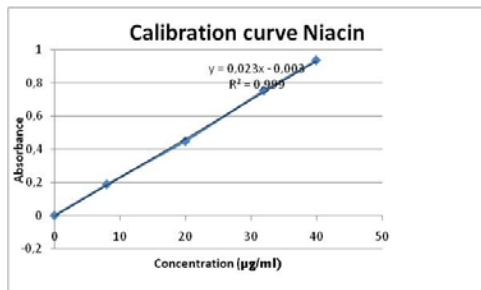
The calibration curve of each vitamin was obtained according to the method described previously. For riboflavin and niacin the correlation coefficient was 0,999. The pyridoxine calibration curve was a linear regression with good correlation coefficient was 0,991.



Graphic 1. The calibration curve of riboflavin



Graphic 2. The calibration curve of pyridoxine



Graphic 3. The calibration curve of niacin

Identification

The identification of riboflavin through UV-Vis spectrophotometer, showed the characteristic spectrum of riboflavin with two peaks, ($\lambda_{\text{max } 1} = 260\text{nm}$, $\lambda_{\text{max } 2} = 430\text{nm}$). The absorbance ratios were: $A_{273}/A_{267} = 0,313$ and $A_{444}/A_{264} = 0,368$. The ratios were within the limits described by the European Pharmacopoeia $A_{273}/A_{267}[0,31-0,33]$; $A_{444}/A_{264}[0,36-0,39]$.

Identification of pyridoxine through the reaction of the aqueous solution of powdered tablets with ferric (III) chloride showed a deep red color as described in the (2.3.1 EuPh 5.0).

The ratio A_{237}/A_{262} of niacin of the solutions of $20\mu\text{g/ml}$ of each production (Canadian and Albanian tablet) was evaluated to be 0,37 and 0,68 respectively, which fell in the limits range of $[0,35-0,39]$ according to USP.

Weight variation

The weight variation results showed that any of the two productions of B complex vitamin passed the limit of the percentage of deviation of 10% as described in the USP. The results are showed in table 1.

Hardness test

The hardness test results in table 1 showed that the Albanian production had a lower value of hardness compared to the Canadian tablets. The advised value is 4-10 Kpa, otherwise the disintegration test should be conducted, since the hardness test is not a pharmacopeia test.

Disintegration test

According to USP limit, disintegration time of both productions was within the limits of 30min. The results are showed in table1.

	Weight variation (g \pm stdev)	Maximum % deviation	Hardness (kpa \pm stdev)	Disintegration time (min)
Albanian B complex tablet	0,2543 \pm 0,0099	8%	3,66 \pm 0,74	15,46
Canadian B complex tablet	1,3632 \pm 0,0092	1,80%	25,04 \pm 1,73	21,06

Table1. The results for weight variation test (along with the maximum %deviation value calculated), hardness test and disintegration test.

Legislative regulation

The retrospective analysis of legislative regulation in Albania showed that there is no strict difference in what is considered dietary/nutritional supplement and what is considered food. In this gap created, there are can be many dietary supplements (even in high vitamin doses) sold in the Albanian market with no control of the drug authorities.

Conclusion

The quality control tests implemented for the different productions of Albanian and Canadian B-complex tablets ensues that both of the productions fulfill the limits of pharmacopoeia for the presented tests (identification, weight variation, disintegration). In the comparison of these products, it is noticed difference in technological formulation, hardness and packaging.

The retrospective analysis of the legislative framework shows a gap in the marketing and sale protection for these multivitamin tablets as genuine pharmaceutical products. There is a thin line of distinction between food/health supplement and drugs, particularly in a case where the contents and concentration of nutritional value and vitamins are specifically mentioned for various commercial reasons, making the categorization highly subjective. There is also no judicial unanimity in this regard. There is no specific statutory or judicial yardstick available for being decisive on this aspect. That leads to the conclusion that the categorization of health and nutritional supplements as "food supplement" or "drug" would depend on the analysis of the ingredients/composition of the specific supplement as well as subjectivity of the authorities.

The Health Services should make an expertise to analyze the ingredients or components of each drug to know the effect of such drugs on the human body. These kind of analysis, can tell us whether we have a 'drug' or a 'food'.

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