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Quantitative Analysis of Commercial Preparations of Isoniazid

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ABSTRACT

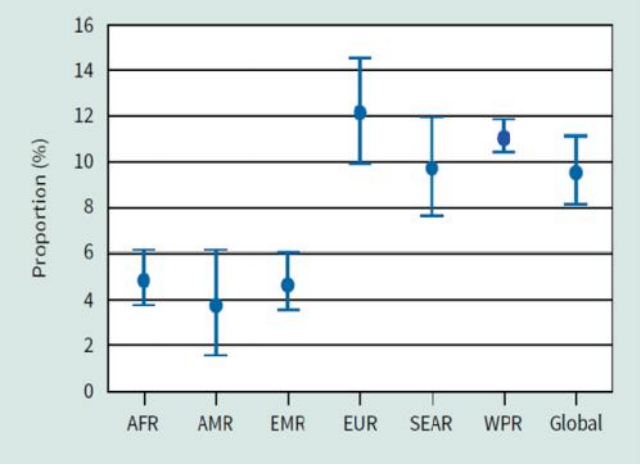
Aim: To quantitatively estimate the strengths of isoniazid in commercial preparations using spectrophotometry. **Methods:** 49 isoniazid tablets of strength of 300 mg were bought from a local pharmacy. Ultraviolet spectrophotometer from the department of Pharmacology was utilised for estimation of actual tablet strength using the method described by Enoch Florence Oga.(1) **Results:** A total of 49 commercially available Isoniazid tablets were estimated in duplicates. The mean and SD for the 49 tablets was estimated as 295.2±12.2 mg. **Conclusion:** The strength of all Isoniazid tablets from commercial preparations were within normal range of 90 to 110% as prescribed by WHO.

Keywords: Isoniazid, UV-Spectrophotometry, Quantitative estimation, Commercial preparations

INTRODUCTION

Tuberculosis ranks as one of the top ten causes of death in the world. In the latest data provided by the World Health Organisation, in 2016, 10.4 million people had acquired the disease and 1.7 million succumbed to it. Among the deaths, 95% were from low and middle-income nations. Of the total number of cases of tuberculosis worldwide, 64% cases are accounted by seven nations, namely Indonesia, China, Philippines, Pakistan, Nigeria and South Africa with India leading the list. Tuberculosis is also the prime killer among the HIV patients, 40% of deaths in this category of patients in 2016 were due to tuberculosis. (2) India alone is responsible for one fourth of the global TB cases. It also has the highest burden in terms of multi drug resistant cases and ranks second in the number of HIV associated TB cases.(3)

New patients with pulmonary tuberculosis are treated with two months of intensive therapy with isoniazid, rifampicin, ethambutol and pyrazinamide and four months of continuation therapy with isoniazid and rifampicin. Anti-TB medications have been used for the last several years, but resistant bacterial strains have been noted to one or more of these medications in every country surveyed. Resistance to anti-TB medications occur when they are used inappropriately, either due to wrong prescriptions given by doctors, the substandard quality of the drugs supplied or due to patients not being compliant with their medicines. Multi-drug resistance is due to bacterial resistance to the most powerful of the first line agents, isoniazid and rifampicin. Among all the patients with tuberculosis, resistance to isoniazid without that to rifampicin accounts to 9.5%. Among the INH resistant patients, the new cases account for 8.1% of the world average and the previously treated patients account for 14%. (4)



AFR : Africa AMR : America EMR :Eastern Mediterranean EUR : Europe SEAR : South East Asia WPR : Western Pacific Region

Figure 1 : Proportion of all TB cases with resistance to INH and not to rifampicin by WHO region, 1994-2013(4)

With availability of Xpert MTB/RIF testing, it is vital to note that around 1 in 10 patients on an average in the population who are still sensitive to rifampicin may be resistant to isoniazid and this can't be detected by this test. Patients who are treatment failures need to be checked for resistance to both isoniazid and rifampicin.(4) Multi-drug resistant TB takes a longer period of time for treatment, an approximate of 2 years with drugs which have serious side effects (5) and estimates of mean costs per patient amounting to 4.8 lakhs.(6)

Not only in treatment, but isoniazid therapy forms the backbone of preventive therapy in children below 6 years of household contacts and in people living with HIV/AIDS in whom active TB has been ruled out. (3)

WHO in its' recent report has stated that, 1 in 10 medical products being circulated worldwide, especially in the low or middle-income countries are either substandard or falsified. WHO defines substandard drugs as "Authorised medical products that fail to meet either their quality standards or specifications, or both". Falsified medical products are defined by WHO as "Medical products that deliberately misrepresent their identity, composition or source."(7) Among these drugs, antimalarials and antimicrobials rank the highest. These substandard or falsified medicines not only have a devastating consequence on individuals, but these individuals are also at a risk of development of resistance. WHO is reporting studies which show that there is a 10.5% failure rate in drugs manufactured, mainly in low and middle income countries.(8)

With the growing rate of antimicrobial resistance, it is imperative to check the quality of anti-TB medicines. Despite, the contribution of poor quality medicines to resistance, the global prevalence of substandard ant-TB medications has not been properly assessed. This is because the nations with the highest cases of tuberculosis don't have good quality laboratory facilities to test for substandard and falsified medicines. Lack of well trained staff and the high cost of equipment like HPLC and UV-spectrophotometry used in analysing ant-TB medicines are the reasons quoted for inadequate data on quality of medicines in these areas.(9)

In our study, we aim to measure quantitatively the strengths of Isoniazid tablets using a simple method of estimation.

MATERIALS AND METHODS

This study was approved by the Institutional review board of Christian Medical College, Vellore (IRB Min. no. 10577). The study was done in the Department of Pharmacology, Christian Medical College, Vellore.

The Isoniazid tablets of the same manufacturer were bought over the counter without a prescription from a local pharmacy for the analysis. The Isoniazid pure powder was obtained from Sigma Aldrich India and the vanillin powder was obtained from the department of Pharmacology, CMC Vellore.

Each tablet was from a single brand and the tablets were of strength 300 mg. Tablets of strength 100 mg, tablets after expiry, fixed drug combinations and tablets of inadequate labels were excluded. The purchased tablets were stored in the refrigerator and testing was completed within 10 days of tablet purchase. Each tablet strength was estimated as per the procedure described by Enoch Florence Oga, as follows. (1) 100 ml of Isoniazid stock was prepared at a concentration of 1mg/ml using Isoniazid pure powder. 3 working standards of 100 µg/ml, 400 µg/ml, 600 µg/ml and a quality control of 200 µg/ml were prepared from the standard stock. The quality control was prepared to ensure accuracy of the methodology. Isoniazid tablets were then crushed and dissolved in 100 ml of distilled water and was considered as unknown, subjected for estimation. After dissolving, the solution was poured into two test tubes as each tablet was estimated in duplicates to avoid errors. 5 ml of each aliquot of Isoniazid was taken, to which 4 ml of 3% vanillin was added which was separately prepared fresh. To this mixture 8 ml of 0.5 M ethanol hydrochloric acid was then added. This solution was then allowed to stand for 10 minutes. The absorbance of the yellow coloured solution was taken at 405 nm against a reagent blank and working standards in the spectrophotometer (Lab India Analytical Instruments Pvt. Ltd., Gurgaon, India). An absorbance concentration graph was plotted with the standard and test aliquots and then the % age strength of each tablet was obtained using the straight -line equation. Fig. 2 shows the calibration curve obtained in the spectrophotometer.

A drug sample was defined as substandard by spectrophotometry if it had less than 90% or more than 110% of the reference standard as defined by WHO.(9)

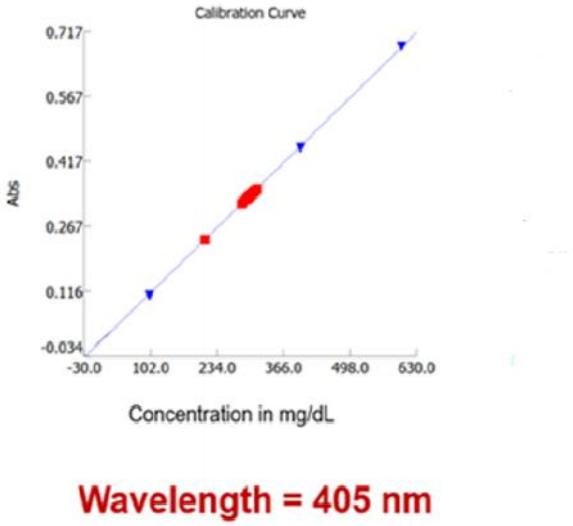


Figure 2: Spectrophotometer calibration curve

RESULTS

A total of 49 Isoniazid tablets were estimated in duplicates. Descriptive statistics was used to analyse the data. Majority of the tablets were between 280-300 mg as shown in Fig. 3. The mean and SD for the 49 tablets was estimated as 295.2±12.2 mg. (Fig. 4) All the tablets conformed to the acceptable standards as stipulated in the WHO reference standard for Isoniazid (90-110% or 270-330 mg).(10)

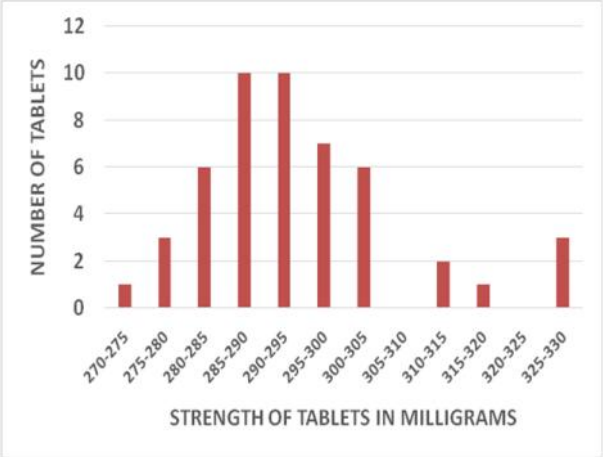


Figure 3: Categorical data on Isoniazid tablet strength in the commercial preparation

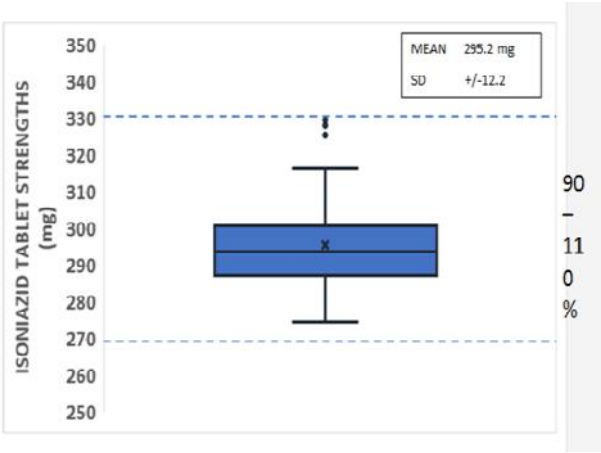


Figure 4: Box plot showing mean and SD of tablet strengths

DISCUSSION

Isoniazid is one of the first line anti-TB drugs used in prevention and treatment of tuberculosis. India bearing such a great burden of the disease(3), it is imperative that good quality drugs are supplied to the general population.

In a report by the European commission, it was stated that 75% of the substandard drugs came from India. In the year 2000, it was noted that 35% of the global sales of counterfeit drugs came from India. (11)

A pilot study done on essential drugs in two major cities in India, Delhi and Chennai showed that 12% of isoniazid samples tested failed the quality standards.(12) Another study done on Isoniazid and Rifampicin by Bates et al showed a 10% failure in quality standards in India.(13) In 2007-2008, the leading numbers in development of spurious drugs was Maharashtra with Kerala leading in the next two years.(11)

In spite of all the data that has come out on spurious drugs, there have not been many studies done extensively on the quality of drugs in the market.(11) In our study though, all the tablets were within the quality standards as defined by the WHO. This is reassuring to note, though it cannot be generalised as the sample size was small and samples were taken from a single pharmacy.

In a country like India where there aren't adequate facilities to test drugs using HPLC due to lack of inadequately trained staff, our study highlights the fact that a method like spectrophotometry, which is cheap and does not require well trained staff and which can be made available in primary/ secondary health care centres can be used to test the quality of drugs and ensure the safe supply of standard quality drugs to our general population.

CONFLICT OF INTEREST

There are no conflicts of interest from the part of the part of the contributing authors. An intramural fluid grant, Christian Medical College, Vellore, was received for the work.

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