Acta Tropica 177 (2018) 157–163

Contents lists available at ScienceDirect

Acta Tropica

journal homepage: www.elsevier.com/locate/actatropica

Quality of anthelminthic medicines available in Jimma Ethiopia

Sileshi Belew[a,b], Sultan Suleman[b], Evelien Wynendaele[a], Matthias D'Hondt[a], Anne Kosgei[a], Luc Duchateau[c], Bart De Spiegeleer[a,*]

[a] Drug Quality and Registration (DruQuaR) Group, Faculty of Pharmaceutical Sciences, Ghent University, Ottergemsesteenweg 460, B-9000 Ghent, Belgium
[b] School of Pharmacy, Jimma University, PO Box 378, Jimma, Ethiopia
[c] Department of Biometrics, Faculty of Veterinary Medicine, Ghent University, Salisburylaan 133, B-9820 Merelbeke, Belgium

ARTICLE INFO

Keywords:
Anthelminthics
Ethiopia
Pharmaceutical quality
Survey

ABSTRACT

Soil-transmitted helminthiasis and schistosomiasis are major public health problems in Ethiopia. Mass deworming of at-risk population using a single dose administration of 400 mg albendazole (ABZ) or 500 mg mebendazole (MBZ) for treatment of common intestinal worms and 40 mg of praziquantel (PZQ) per kg body weight for treatment of schistosomiasis is one of the strategies recommended by World Health Organization (WHO) in order to control the morbidity of soil-transmitted helminthiasis and schistosomiasis. Since storage condition, climate, way of transportation and distribution route could all affect the quality of medicines, regular assessment by surveys is very critical to ensure the therapeutic outcome, to minimize risk of toxicity to the patient and resistance of parasites. Therefore, this study was conducted to assess the pharmaceutical quality of ABZ, MBZ and PZQ tablet brands commonly available in Jimma town (south west Ethiopia). Retail pharmacies (n = 10) operating in Jimma town were selected using simple random sampling method. Samples of anthelminthic medicines available in the selected pharmacies were collected. Sample information was recorded and encompassed trade name, active ingredient name, manufacturer's name and full address, labeled medicine strength, dosage form, number of units per container, dosage statement, batch/lot number, manufacturing and expiry dates, storage information and presence of leaflets/package insert. Moreover, a first visual inspection was performed encompassing uniformity of color, uniformity of size, breaks, cracks, splits, embedded surface spots or visual contaminations. Finally, physico-chemical quality attributes investigated encompassed mass uniformity, quantity of active pharmaceutical ingredient (API), disintegration and dissolution, all following Pharmacopoeial test methods The physical characteristics of dosage form, packaging and labeling information of all samples complied with criteria given in the WHO checklists. The mass uniformity of tablets of each brand of ABZ, MBZ and PZQ complied with the pharmacopoeial specification limits, i.e no more than 2 individual masses > 5% of average tablet weight, and none deviate by more than 10%. The quantity of APIs in all investigated tablet brands were within the 90–110% label claim (l.c.) limits, ranging between 95.05 and 110.09% l.c. Disintegration times were in line with the pharmacopoeial specification limit for immediate release (IR) tablets, ranging between 0.5 and 13 min. However, the dissolution results (mean ± SD, n = 6) of one ABZ brand (i.e. Wormin®, Q = 59.21 ± 0.99% at 30 min) and two PZQ brands (i.e. Bermoxel®, Q = 63.43% ± 0.7 and Distocide®, Q = 62.43% ± 1.67, at 75 min) showed poor dissolution, failing the United States Pharmacopoeia (USP) dissolution specification limit.

1. Introduction

Neglected tropical diseases (NTDs) are affecting 500 million people living in Sub-Saharan Africa countries. In this region, NTDs are annually causing an estimated 534, 000 deaths and 57 million disability-adjusted life years loss (Conteh et al., 2010). Ethiopia is one of the Sub-Saharan Africa countries, where different NTDs mainly schistosomiasis and soil-transmitted helminthiasis are affecting millions of people living in endemic areas (Bajiro et al., 2016; Bitew et al., 2016; Dana et al., 2014; Mengistu et al., 2011). The prevalence of soil-transmitted helminths and schistosomiasis in Ethiopia is 48–52% (Tefera et al., 2017; Mekonnen et al., 2016) and 31–81% (Tadege and Shimelis, 2017; Bereket and Zewdneh, 2015), respectively. To reduce morbidity and eliminate NTDs by 2020, the World Health Organization (WHO)

* Corresponding author.
E-mail addresses: sbphar2009@gmail.com (S. Belew), sultan.suleman@ju.edu.et (S. Suleman), Ejwynend.Wynendaele@UGent.be (E. Wynendaele), Matthias.DHondt@UGent.be (M. D'Hondt), Anne.Kosgei@UGent.be (A. Kosgei), Luc.Duchateau@UGent.be (L. Duchateau), Bart.Despiegeleer@UGent.be (B. De Spiegeleer).

http://dx.doi.org/10.1016/j.actatropica.2017.10.006
Received 30 June 2017; Received in revised form 15 September 2017; Accepted 7 October 2017
Available online 13 October 2017
0001-706X/

recommends mass drug administration for at-risk populations as one of the best strategies (WHO, 2010). However, in low-income and middle-income countries, high prevalence of poor quality medicines (Caudron et al., 2008; Cohn et al., 2012; Fadeyi et al., 2015; Suleman et al., 2014) and failure of pharmaceutical distributors to apply stringent criteria for selecting products and suppliers (Giralt et al., 2017), are prevailing challenges in patient's access to quality medicines.

In Ethiopia, the existing weak regulatory enforcement, lack of informal market control, weak port control, poor cooperation between executive bodies and resource constraint (Suleman et al., 2016) and long border that Ethiopia shares with neighbouring countries, could contribute to infiltration of poor quality medicines into the pharmaceutical supply chain. Since poor quality of medicine is linked with reduced efficacy (Belew et al., 2015; Lacey, 1990; Leslie et al., 2009) and toxicity to patients (Peyraud et al., 2017), evaluating the quality of essential medicines is crucial for delivering quality health services. In Ethiopia, owing to the prevalence of schistosomiasis and soil-transmitted helminthiasis as well as other parasitic worms, different brands of anthelminthic medicines are indiscriminately used in the treatment of parasitic infections. However, there is little information about the quality of these medicines circulating in the market (Belew et al., 2015; Suleman et al., 2014). Therefore, this study was conducted to assess the quality of anthelminthic medicines encompassing ABZ, MBZ and PZQ tablets brands commonly available in legally operating retail pharmacies in Jimma town.

2. Materials and methods

2.1. Survey area

The survey was conducted in Jimma town. Jimma town is located at 352 km from the capital Addis Ababa. According to Central Statistical Agency (CSA) report the projected population of Jimma zone from 2014 to 2017 is estimated to be 2,986,957 (CSA, 2013). Jimma is a relatively large town with nine legally operating wholesalers of pharmaceutical products which are currently supplying pharmaceutical products to retail pharmacies (n = 22), health centers (n = 4), clinics (n = 15) and hospitals (n = 2).

2.2. Sample collection

From a total of 22 pharmacies officially operating in Jimma town, 10 pharmacies were selected using simple random sampling method. One box of anthelminthic was bought in each of retailing pharmacy resulting in samples for quality verification. One pharmacy did not have one of the requested anthelminthics. All samples were transported to Jimma University Laboratory of Drug Quality (JuLaDQ) on the same day of sample collection. In addition, survey on the sales volume and price of ABZ, MBZ and PZQ products available in legally operating wholesalers (n = 9) and retail pharmacies (n = 22) was conducted.

2.3. Chemicals/reagents/solvents

ABZ (USP reference standard), MBZ (Janssen Pharmaceutica) and PZQ (Sigma-Aldrich) reference standards were used as received. Hydrochloric acid (37% w/v, Sigma-Aldrich), methanol (HPLC grade, Fishers Scientific), acetonitrile (HPLC grade, Fishers Scientific), orthophosphoric acid (Fluka Chemicals Ltd.), potassium phosphate monobasic (KH_2PO4) (Sigma-Aldrich), ammonium phosphate monobasic (Sigma-Aldrich), sodium hydroxide (Sigma-Aldrich), sodium lauryl sulphate (Sigma-Aldrich) and ultra pure water (18.2 Ωcm) were used.

2.4. Physical characteristics, packaging and labelling information

Visual inspection of the physical characteristics of dosage form, packaging and labelling information was performed following the WHO checklist (WHO, 2015) designed to health professionals to carry out visual inspection of medicines for signs of counterfeiting and report to appropriate national authority or directly to WHO. All samples underwent visual inspection for trade name, active ingredient name, the manufacturer's name and full address, labeled medicine strength, dosage form, number of units per container, dosage statement, batch/lot number, manufacturing and expiry dates, storage information, presence of leaflets/package insert. Moreover, a first visual inspection was performed encompassing uniformity of color, uniformity of size, breaks, cracks, splits, embedded surface spots or visual contaminations. Finally, samples were stored between 21.6 °C ± 1.09 as minimum and 22.09 °C ± 0.89 as maximum daily average temperature (mean ± SD, n = 119 days,), with a relative humidity (%RH) of 36.63% ± 7.04 until analysis.

2.5. Mass uniformity

The mass uniformity test was performed according to the method given in European Pharmacopoeia (Ph. Eur., 2014a). Randomly selected tablets (n = 20) from each brand of ABZ (Albenzole®, Ovis® and Wormin®), MBZ (Mebepharm®, Wormin® and Thelmox®) and PZQ (Bermoxel®, Distocide® and Praziquantel) were weighed using a calibrated analytical balance (Mettler Toledo, AB204-5, Switzerland). The average weight was calculated and the mass uniformity of tablets was evaluated against Pharmacopoeia specification limit (i.e. no more than 2 individual masses > 5% of the average tablet weight, and none deviating by more than 2 × 5% of the average tablet weight).

2.6. Amount of API

2.6.1. System suitability

System suitability test was evaluated according to European Pharmacopoeia method (Ph. Eur., 2014b). The symmetry factor of principal peak of reference standard and percent relative standard deviation of replicate injections (6 times) of reference standard were calculated and compared against Pharmacopoeia specification limit i.e symmetry factor of the principal peak (0.8-1.5) and maximal permitted percent relative standard deviation (%RSD) of replicate injections (0.85).

2.6.2. Albendazole

The amount of API of samples of ABZ tablets was investigated according to the United States Pharmacopoeia method (USP, 2015a).

2.6.2.1. Preparation of standard solution. Approximately 100.0 mg of ABZ reference standard (RS) was accurately weighed into a 50.0 mL volumetric flask and dissolved in 5.0 mL of acidified methanol (sulfuric acid/methanol, 1/99% v/v). The prepared stock solution was diluted with methanol to volume and mixed. A volume of 5.0 mL of the solution was transferred into a second 50.0 mL volumetric flask and diluted with methanol to volume and mixed again.

2.6.2.2. Preparation of sample solution. Randomly selected tablets (n = 20) were finely powdered. A portion of powder equivalent to approximately 100.0 mg ABZ was transferred into a 50.0 mL volumetric flask, dissolved in 5.0 mL of acidified methanol (sulfuric acid/methanol, 1/99% v/v), shaken for 15 min, diluted with methanol to volume, mixed and filtered with Whatman No. 1 filter paper by discarding the first 15.0 mL of the filtrate. A 5.0 mL of clear filtrate was transferred into a second 50.0 mL volumetric flask, diluted with methanol to volume and mixed.

2.6.2.3. HPLC method. The samples were analyzed using HPLC equipped with a 254 nm UV–vis detector and a C18 column (4.6 mm x 25 cm, 5 µm) (Zorbax, Agilent). The mobile phase was a mixture of 0.50 g monobasic ammonium phosphate ($NH_4H_2PO_4$) in 400.0 mL