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In Vitro Biopharmaceutical Quality Control of Risperidone (2 mg) Tablets and Their Impact on Public Health

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ABSTRACT

Introduction: Innovative and similar branded medications are expensive and are not accessible in the poorest sectors of Peru, hence the importance of having bioequivalent generic medications. This study aims to evaluate the in vitro biopharmaceutical quality of risperidone 2-mg tablets and their impact on public health. **Methods:** Four brands of risperidone from the local market were studied (two generic [G1T, G2A], one similar [M1], and one reference [R1]). An analytical and experimental study was conducted using a spectrophotometric method for the dissolution profile in a United States Pharmacopeia (USP) apparatus 2 at 50 rpm with 500 mL of dissolution medium at pH 1.2, 4.5, and 6.8, at 37 ± 0.5 °C. Weight, hardness, and friability were also evaluated. Similarity factor (f_2), dissolution efficiency, and mean dissolution time were used as statistical indicators of biopharmaceutical quality control. **Results:** At pH 1.2 and 4.5, the generic (G1T, G2A) and similar (M1) products did not release more than 85% of the drug within 15-30 min. API release at pH 1.2 was 73.53–74.99% and 75.82–76.64% at 15 and 30 min, respectively. At pH 4.5, API release was 54.92–66.25% and 57.50–75.25% at 15 and 30 min, respectively. In the basic dissolution medium (pH 6.8), the dissolution percentages were 81.99–105.43% at 15 min and 88.32–107.24% at 30 min. When compared to the reference brand, the f_2 values in pH 1.2, 4.5, and 6.8 were 55.42, 47.21, and 58.75 for G1T, respectively; 47.51, 28.63, and 24.33 for G2A; and 47.16, 31.51, and 27.68 for M1. The dissolution profiles for G2A and M1 presented differences of 15% at pH 1.2 and more than 20% at pH 6.8. Dissolution efficiency at pH 1.2 and 6.8 was greater than 77%, and mean dissolution time was less than less than 25.29 min. All formulations met the quality control attributes of the biopharmaceutical phase (weight, hardness, and friability). **Conclusion:** Only one of three generic medicines (G1T) was considered biopharmaceutically equivalent to the reference brand in vitro in both acidic and basic dissolution medium.

Keywords: Risperidone, biopharmaceutical equivalence, dissolution profile, generic drug, reference drug

INTRODUCTION

For any given medication, three types of products may be marketed throughout the world: the *innovator* (original), *similar* (medications manufactured by different laboratories with commercial names) and *generic* (*1, 2*). Innovative medications and even similar ones are high cost, so they have limited access in the sectors with fewer economic resources in Latin America and

especially in Peru, hence the importance of replacing them with bioequivalent generic drugs (*1, 3*). Bioequivalence can be demonstrated through in vivo or in vitro studies, depending on the health risk. By demonstrating relative bioavailability, the in vivo bioequivalence of high health risk drugs that belong to Biopharmaceutical Classification System (BCS) *class 2* (low solubility and high permeability) and *class 4* (low solubility and low permeability) is established (*4*). For *class 1* (high solubility and high permeability) and *class 3* (high solubility and low permeability) drugs, bioequivalence is demonstrated through in vitro studies in three dissolution mediums at pH 1.2, pH 4.5, and pH 6.8 that simulate the physiological conditions of the gastrointestinal tract to predict optimal absorption (and these studies are economical and fast) (*5–7*). Overall, bioequivalence studies can guarantee the similarity of the dissolution profile as well as safety and efficacy (and therapeutic interchangeability) of generic and similar medications relative to the innovator (or reference) medication (*5, 8, 9*).

Risperidone is one of the most used antipsychotics in the treatment of mental disorders due to its safety compared to other antipsychotics (*10*). This drug is BCS class 2, meaning that the dissolution rate is the limiting factor for its absorption (*11*). Risperidone is structurally derived from benzisoxazole and has a basic pKa (pKa_1 8.76; pKa_2 1.16); it is predominantly absorbed in the intestinal mucosa, because it is found in a higher percentage in its non-ionized form (*12*). The efflux transporters ABCB1 (glycoprotein P-170) of the enterocyte decrease the absorption of risperidone, being metabolized by CYP3A4/CYP2D6 during the first pass effect, reaching a bioavailability of 60–70% (*12–14*). The maximum plasma concentration (C_{max}) of the original molecule and its active metabolite (+)-9-hydroxyrisperidone (paliperidone) is 20–60 ng/mL; this concentration is reached in a maximum time (t_{max}) of 1–3 h, respectively (*12, 15*). The average stable concentration (C_{ss} = 10 ng/mL) is reached in 7 days; the free fraction and its active metabolite circulate and bind to albumin and α_1 acid glycoprotein in 90% and 77.4%, respectively; and the volume of distribution (Vd) is 0.9–2 L/kg (*12*). Through phase I oxidation, risperidone is metabolized by hydroxylation: with participation of *CYP2D6*, paliperidone is generated, and by *CYP3A4*, it is biotransformed into (-)-9-hydroxyrisperidone (*12, 16*). N-dealkylation produces N-dealkylated metabolites by the action of *CYP3A4* and *CYP3A5* (*12*). By phase II of glucuronidation, the hydroxylated metabolites are biotransformed into O-β-glucuronide of risperidone; to do this, UDP-glucuronosyl transferase (UGT) transfers a glucuronic group from UDP-α-D-glucuronic acid (UDPGA) to the drug. The half-life ($t_{1/2}$) is 22 hours, which varies according to the patient's metabolic phenotype, and its conjugated metabolite is eliminated through the kidneys (*12, 14*).

Immediate-release solid oral dosage forms are targets of in vivo and in vitro correlation studies following the BCS guidelines for class 1 and 3 drugs (*11, 17*). In this sense, it is important to evaluate the biopharmaceutical phase that includes disintegration (which can be macrogranular or microgranular), dissolution, and absorption by simple diffusion. Disintegration and dissolution depend on technological and formulation factors; the dissolution phase is the limiting stage of absorption. Absorption depends on physicochemical and physiological factors and first-pass metabolism or presystemic effect. Through in vitro biopharmaceutical equivalence studies, disintegration, friability, hardness, and dissolution of immediate-release solid oral pharmaceutical forms are evaluated (*6*).

It is justified to carry out in vitro biopharmaceutical studies and bioequivalence of risperidone in Peru for four reasons. First, these studies contribute to the quality control of class 2 drugs; and through in vitro bioequivalence studies for multisource class 1 and 3 drugs, equivalence with the reference drug is guaranteed by demonstrating that more than 85% of the active pharmaceutical

ingredient (API) is released within 15–30 min. Second, through biopharmaceutical quality control studies, the quality, efficacy, and safety of medicines in the Single National Petition for Essential Medicines of the Ministry of Health are guaranteed (*4*). Third, the Peruvian population is of tricontinental and Latin American ancestry, so it is of vital importance to carry out relative bioavailability studies considering the genetic polymorphism (*CYP2D6*, *CYP2C9*, *CYP3A4*, *CYP1A1*, and others) and metabolic phenotype that influence in the bioavailability and serum level of the drug as a potential cause of therapeutic failure, adverse effect, and/or toxicity (*18–22*). Fourth, through in vitro biopharmaceutical quality control studies, drugs of dubious origin and falsified (without API) and low quality (with insufficient quantities of API) drugs are identified, helping to mitigate this global public health problem (*4, 5, 23*). Therefore, this study aims to evaluate the in vitro biopharmaceutical quality of risperidone 2-mg tablets and how the results impact public health. To this end, statistical indicators of equivalence were applied such as the similarity factor (f_2), dissolution efficiency (DE%), and mean dissolution time (MDT).

METHODS

Materials

The study sample comprised four brands of 2-mg risperidone (200 tablets of each): two generic brands, one similar brand, and the reference brand. All products were acquired in a local pharmacy in Lima, Peru. The experimental phase was carried out double-blind, therefore, each formulation was randomly coded with letters: Generic "G1T" (lot 20600242, RS EN-01738, expiration 05/2025, AC FARMA); generic "G2A" (lot 2100221, RS EN-05070, expiration 03/2026, LAFARMA); and similar "M1" (lot 2011744, RS EN-04043, expiration 01/2027, ABPharma). The reference drug Zepidona was coded as "R1" (lot ST 22-2521, RS EE-09437, expiration 10/2024, Health Care Laboratory). All trials were performed within the shelf life of the drugs.

The reagents used were of American Chemical Society and analytical grade. These included hydrochloric acid 37% (EMSURE, Germany), sodium hydroxide (EMPLURA, Germany), anhydrous sodium acetate 99.65% (J.T. Baker, USA), and monobasic potassium phosphate 99.63% (J.T. Baker, USA), which were obtained from Mercantil SAC (Lima, Peru), as well as USP Risperidone Standard (Sigma-Aldrich, USA), and Chromafil syringe filters (25-mm size, 0.45-µm pores).

Technique Validation and Equipment Calibration

The dissolution method was validated using 50-mg propylthiouracil tablets by spectrophotometry (Unico Spectrophotometer Model UV 2100 Series, USA) at 239 nm. The parameters evaluated were specificity, to find interference between the API and excipients in the tablets; linearity (range 1.60–7.75 µg/mL); and precision, performed every other day and with six tablets (*4, 5, 8, 9*).

Calibration of the dissolution tester (Electrolab ETC-11Lx, Model 1104197, Series 1201044, India) was performed with USP 10-mg Prednisone RS tablets (lot R080J1) using 500 mL of purified water as a dissolution medium at 37 ± 0.5 °C for 30 min. The distance between the bottom of the paddle and the bottom of the dissolution vessel was 25 ± 2 mm. The temperature selector was set to 37 °C to qualify the isothermal medium, the uniformity of the heat of the water bath was verified, which heats the distilled water surrounding the dissolution vessel and the purified water inside the vessel by thermal convection (*4, 5, 8, 9*).

Weight Variation, Hardness, and Friability Tests

For weight variation determination, 20 tablets were randomly selected from each product and were immediately weighed individually on an analytical balance (Boeco BBL31, Germany), with the

acceptance criterion being a coefficient of variation less than 4% (*5, 24, 25*).

For hardness tests, 20 tablets were randomly selected from each product. The tablet hardness was determined in a hardness tester (BIOBASE THAT-3, China), with an acceptance limit of 6 ± 2 kg-f (*5, 24, 25*).

For friability, 20 tablets were randomly selected from each product and weighed (W_1). Those tablets were placed in a friability tester (Erweka TAR, Germany) programmed at 25 rpm for 4 min. After this process, the tablets were dusted and weighed again (W_2). The acceptance percentage due to friction loss was calculated with the following equation: $[(W_1 - W_2) \div (W_1 \times W_2)] \times 100$. The acceptance criterion was established less than 1% weight loss (*5, 24, 25*).

Dissolution Test

To obtain the dissolution profile, six tablets from each product were used for evaluation. USP apparatus 2 (paddle) was used at 50 rpm with 500 mL of dissolution medium at three pH (HCl pH 1.2, acetate buffer pH 4.5, and phosphate buffer pH 6.8), maintained at 37 ± 0.5 °C for 90 min. Deaeration of the dissolution medium was carried out under vacuum and on a water bath in ultrasound (Lab Companion, UC-10, series JT-11AB-078-YP, Korea). The dissolution medium was sampled (5 mL) at 5, 10, 15, 30, 45, 60, and 90 min using syringes with 0.45-µm chromafil filters without replacement of dissolution medium. Absorbance of the samples and the blank (dissolution medium) was determined by ultraviolet (UV)-visible spectrophotometry at a wavelength of 237 nm (*5, 8, 9, 24*). To calculate the concentration and percentage of content, a calibration curve was made with an R^2 value of 0.99.

Data Analysis

The results were transcribed into a Microsoft Excel spreadsheet, from where they were exported to perform the statistical analysis. As a statistical indicator of in vitro bioequivalence, the similarity factor (f_2), the dissolution efficiency (DE%) and the mean dissolution time (MDT) were used (*5*, *6*, *7*, *24*). DE was determined with the following equation: $(AUC_o^t \times 100) / Q^{\infty} \times t^{\infty}$, where AUC_o^t is the area under the release curve from the initial time to the final time of the experiment; Q^{∞} is the average amount of the drug obtained at the end of the experiment; and t^{∞} is the final time of the experiment.

MDT was estimated with the following equation: $\sum iti\Delta Q(ti)/Q^{\infty}$, where $\sum iti\Delta Q.ti$ is the sum of the intermediate times (*ti*) and increase in the dissolved amounts of dissolved drug ($\Delta Q.ti$); and Q^{∞} is the average amount of the drug obtained at the end of the experiment. GraphPad Prism 9 Statistical Software (version 9.1.2) was used.

RESULTS AND DISCUSSION

The innovator risperidone medication Risperdal was not available in Peru at the time of this study, so a reference medication was selected according to the WHO guideline (*26*). First, based on the WHO guideline, a medication available at the national level should be searched; second, if a reference medication is not available in the country, one from the WHO reference list should be used; third, look for a reference on the list of the International Conference on Harmonization (ICH). If none of the above are available, an appropriate reference (including a generic) that has been shown to be similar in safety, quality, and efficacy to the innovator can be used (*26, 27*). Therefore, for the present study, Zepidona 2-mg tablets from Laboratory Salud Care were used as the reference product.

Variations in risperidone tablet weight, hardness, and friability were evaluated, and the results are presented in Table 1. The percentage of the coefficient of variation (CV%) of the weight was less than 4%, which indicates reproducibility within and between batches of the formulations studied. There are no national or international standards that regulate the weight of solid oral pharmaceutical forms, so the acceptable weight of these formulations is established by the manufacturers (*27*). The hardness test values were below the acceptance criterion (< 6 ± 2 kg-f), indicating low variability and homogeneity within the production batch for each pharmaceutical laboratory. The percentage of friability was less than 1%, demonstrating that the surfaces of the tablets are not susceptible to friction loss and are not easy to crack (*4*, *5*, *8*, *9*, *27*). Together, these results demonstrate that the formulations meet the quality control attributes of the biopharmaceutical phase.

Table 1. Biopharmaceutical Quality Control of Risperidone 2-mg Tablets (n = 20)

Product	Weight Variation, mg (CV < 4%)			Hardness, kg-f (6 ± 2 kg-f)			Friability (< 1%)
	Mean	(± SD)	CV %	Mean	(± SD)	CV%	
R1 (Reference)	155.47	0.434	0.279	4.68	0.124	2.648	0.13
G1T (Generic)	155.55	0.842	0.541	5.30	0.122	2.316	0.16
G2A (Generic)	111.71	0.928	0.831	5.24	0.082	1.578	0.18
M1 (Similar)	210.75	0.818	0.388	5.73	0.012	0.216	0.12

CV: coefficient of variation.

The excipients declared in the inserts of the risperidone formulations are described in Table 2. Excipients comprise the largest percentage of the formulation and may influence the biopharmaceutical release process (disintegration and dissolution). Microcrystalline cellulose (declared in formulations G1T, G2A, and M1) is used for its high compressibility, compactness, improving disintegration, and for its pleasant flavor. Povidone K30 USP (also called polyvinylpyrrolidone or PVP; declared in the R1 formulation) is a soluble polymer with good flow and used as a binder to give hardness to medications with little friability (*28*). Sodium starch glycolate is the sodium salt of carboxymethyl starch ether or cross-linked carboxymethyl starch ether (R1 and G2A, 2–8% w/w); and croscarmellose sodium is a cross-linked sodium carboxymethylcellulose (G1T, 2–5% w/w), which are considered highly effective disintegrants at these concentrations (*29*, *30*). Pregelatinized starch (M1 formulation) swells strongly and is used for hygroscopic drugs as a stabilizer, for moisture-sensitive drugs as a disintegrant, and for its pH-independent dissolution (*28*).

Table 2. Excipients Declared in Insert of Risperidone 2-mg Tablets

Product	Binder and Adherent	Disintegrant	Non-Stick Agent	Lubricant	Diluent
R1 (Reference)	Povidone K30 USP	Sodium starch glycolate type A	Magnesium stearate*	Purified talc*	Calcium sulfate dihydrate
G1T (Generic)	Microcrystalline cellulose	Croscarmellose sodium	Magnesium stearate	Polyethylene glycol	Lactose monohydrate
G2A (Generic)	Microcrystalline cellulose	Sodium starch glycolate type A	Magnesium stearate, silicon dioxide	Polyethylene glycol	Lactose monohydrate
M1 (Similar)	Microcrystalline cellulose	Pregelatinized starch	Magnesium stearate, silicon dioxide	Sodium lauryl sulfate	Lactose monohydrate

**Acts as non-stick agent and/or lubricant.*

Regarding the dissolution profiles, Figure 1 shows examples of an optimal sigmoid curve (Fig. 1A) resulting from uniformity and adequate percentages of excipients used during the manufacturing process, a concave curve (Fig. 1B) resulting from a higher percentage of disintegrants in relation to binders, and a convex curve (Fig. 1C) resulting from a higher percentage of binders that increase the internal forces of the drug molecules and prevent the function of the disintegrants. It has previously been described that disintegrants increase the surface area and generate micropores for the entry of water that are then dispersed into the core of the formulation, which disaggregates into macro and microparticles containing excipients that adhere to the API (*31*, *32*). Finally, the API is released into the dissolution medium; therefore, dissolution is considered the limiting phase of in vivo absorption.

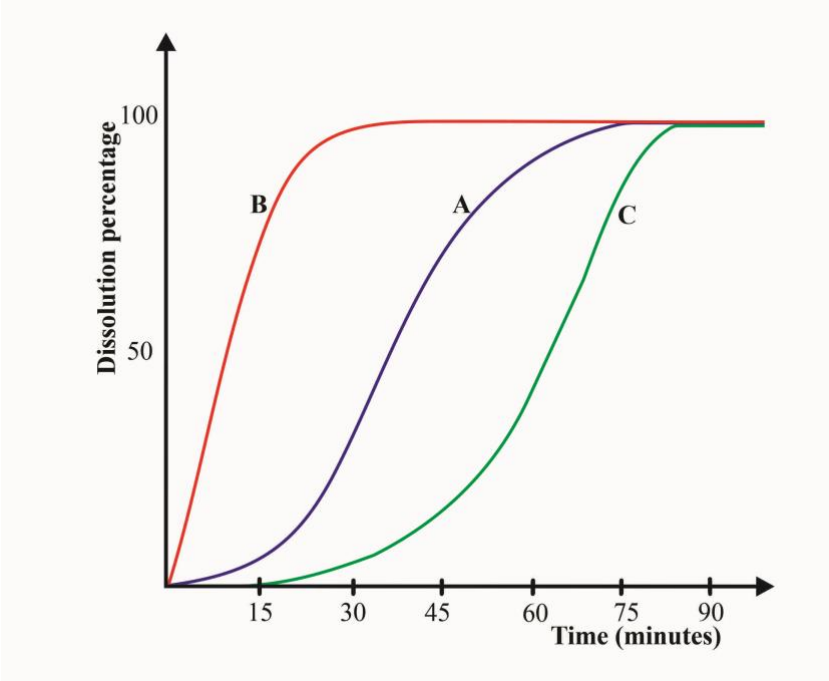

*Figure 1. Examples of dissolution profiles for immediate-release solid oral dosage forms. The sigmoid curve (**A**) indicates an adequate percentage of dissolution, the concave curve (**B**) indicates a higher percentage of disintegrants in relation to binders, and the convex curve (**C**) indicates a higher percentage of binders in relation to disintegrants.*

Results of the dissolution tests for 2-mg risperidone tablets are provided in Table 3 and Figure 2. At pH 1.2 and 4.5, the generic (G1T, G2A) and similar (M1) products did not release more than 85% of drug within 15–30 min. The release of API at pH 1.2 was 73.53–74.99% and 75.82–76.64% at 15 and 30 min, respectively. At pH 4.5, the API release was 54.92–66.25% and 57.50–75.25% at 15 and 30 min, respectively. The percentage of dissolution observed at pH 1.2 would be due to the dissociation constant 2 (pK_2 1.16) of risperidone, indicating that in vivo absorption begins at the gastric level. In the basic dissolution medium (phosphate buffer pH 6.8), the dissolution percentages were 81.99–105.43% at 15 min and 88.32–107.24% at 30 min. This reflects that the main excipients such as disintegrants and binders, are soluble at basic pH. Formulations G2A and M1 showed a higher percentage of dissolution compared to the reference brand, which is due to a reduction in the swelling force, causing high porosity of the tablets. Due to the pKa_1 (8.76) of risperidone, absorption would be optimal at the intestinal level. Dhakal et al. and Berardi et al. have reported that factors that influence disintegration and dissolution are pH of the dissolution medium, solubility of the matrix, and lubricants and surfactants used in pharmaceutical forms (*29*, *33*).

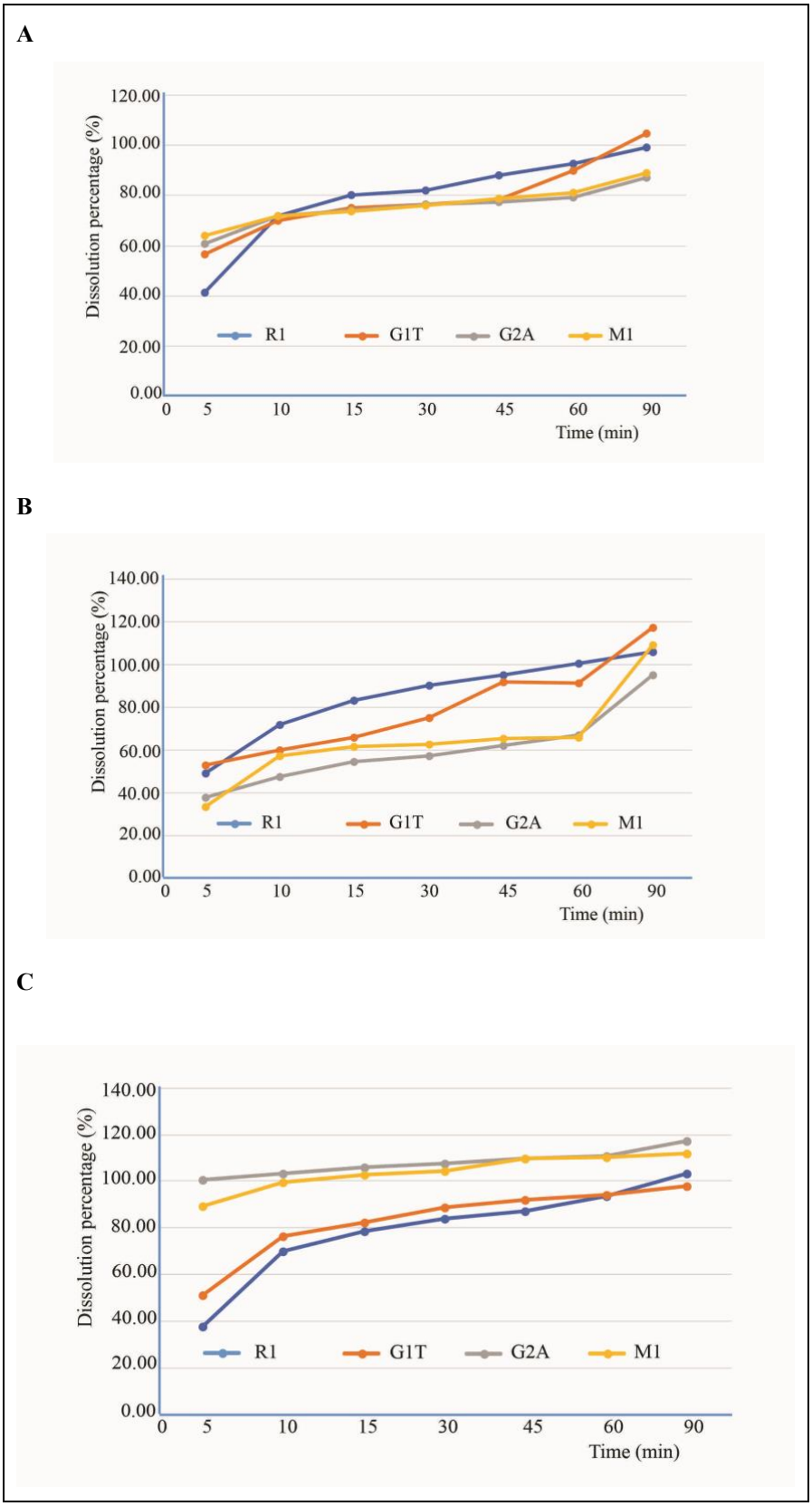

*Figure 2. Observed dissolution profiles for risperidone 2 mg formulations at pH 1.2 (**A**), 4.5 (**B**), and 6.8 (**C**). R1: reference; G1T and G2A: generic; M1: similar.*

Table 3. Dissolution (% drug release) of 2-mg Risperidone Tablets

Time (min)	R1 (Reference)			G1T (Generic)			G2A (Generic)			M1 (Similar)		
	Mean	SD	CV%	Mean	SD	CV%	Mean	SD	CV%	Mean	SD	CV%
Dissolution medium: Hydrochloric acid, pH 1.2												
5	41.17	9.29	22.57	56.29	8.25	14.65	60.60	9.80	16.16	63.72	11.57	18.15
10	71.60	10.86	15.17	69.86	8.32	11.91	71.60	9.70	13.54	71.42	10.35	14.49
15	80.22	1.62	2.02	74.99	11.36	15.15	74.17	10.38	14.00	73.53	10.62	14.44
30	81.87	1.83	2.23	76.37	11.28	14.77	76.64	9.93	12.96	75.82	10.08	13.29
45	88.19	9.49	10.76	78.38	10.98	14.00	77.38	10.37	13.40	78.93	9.31	11.79
60	92.59	7.25	7.83	89.93	20.32	22.60	79.21	10.54	13.30	81.32	8.35	10.27
90	99.10	4.04	4.08	104.69	36.01	34.40	87.18	12.35	14.16	88.83	8.27	9.30
Dissolution medium: Acetate buffer, pH 4.5												
5	49.24	9.32	18.93	53.25	16.72	31.40	37.75	11.78	31.21	33.38	10.86	32.55
10	72.13	5.42	7.51	60.13	10.67	17.75	47.38	12.22	25.79	57.38	13.78	24.02
15	83.25	4.39	5.27	66.25	12.53	18.92	54.92	12.61	22.96	61.50	11.35	18.46
30	90.63	4.62	5.09	75.25	15.69	20.85	57.50	12.38	21.52	62.63	11.36	18.14
45	95.38	6.63	6.95	92.04	18.89	20.52	62.13	14.67	23.62	65.25	11.27	17.27
60	100.63	3.16	3.14	91.63	19.47	21.25	66.88	16.97	25.38	66.00	11.46	17.36
90	106.00	3.49	3.29	117.25	15.87	13.54	95.13	7.48	7.86	109.13	45.64	41.82
Dissolution medium: Phosphate buffer, pH 6.8												
5	37.17	3.40	9.14	50.21	5.34	10.63	100.02	12.18	12.18	88.92	7.97	8.97
10	69.36	2.39	3.45	76.16	18.11	23.77	103.22	15.67	15.18	99.05	3.20	3.23
15	77.82	5.93	7.62	81.99	15.47	18.87	105.43	15.06	14.28	102.24	3.88	3.80
30	83.37	3.96	4.75	88.32	18.32	20.75	107.24	16.91	15.77	104.05	3.80	3.65
45	86.70	3.81	4.40	91.56	17.93	19.59	109.32	17.98	16.44	109.46	0.87	0.80
60	93.22	5.84	6.27	93.92	18.75	19.96	110.57	17.77	16.07	110.15	1.36	1.23
90	102.80	2.34	2.28	97.39	20.62	21.18	111.96	5.49	4.90	111.54	1.39	1.25

SD: standard deviation; CV: coefficient of variation.

Table 4. Similarity Factor (f_2) and Other Parameters that Characterize the Dissolution Profile in the Biopharmaceutical Phase of the API of Risperidone 2-mg Tablets

Product	pH 1.2				pH 4.5				pH 6.8			
	f_2	AUC_o^t (min%)	DE (%)	MDT (min)	f_2	AUC_o^t (min%)	DE (%)	MDT (min)	f_2	AUC_o^t (min%)	DE (%)	MDT (min)
R1 (Reference)	--	7486.73	83.94	18.40	--	8083.67	84.73	17.69	--	7501.35	81.08	21.44
G1T (Generic)	55.42	7295.68	77.43	25.29	47.21	7559.17	71.63	31.84	58.75	7724.00	88.12	14.25
G2A (Generic)	47.51	6802.92	86.70	15.89	28.63	5701.05	66.59	36.91	24.33	9561.12	90.83	11.65
M1 (Similar)	47.16	6895.90	86.26	16.37	31.51	6108.95	62.20	41.67	27.68	9316.37	92.81	9.49

API: active pharmaceutical ingredient; AUC_o^t: area under the release curve; MDT: mean Dissolution Time; DE: dissolution efficiency.

Table 4 shows the parameters that characterize the similarity of the obtained dissolution profiles. A tablet that releases more than 63.2% (DE) of API in the dissolution medium ensures contact with the intestinal mucosa for absorption, and 90% DE indicates optimal dissolution; additionally, the API release must occur within the first 30 min to ensure a direct correlation with the degree of in vivo drug absorption (*8*, *26*, *27*). All DE values were higher than 63.2% except M1 at pH 4.5, which was 62.20%. The MDT indicates at what speed the solid medication dissolves in the dissolution medium, which correlates with average gastric emptying (i.e., mean residence time), which under fasting conditions is 15–20 min (*8*, *26*, *27*). The MDT for G2A and M1 was below 20 min in the acidic dissolution medium (pH 1.2), whereas for G1T it was 25.29 min, indicating slower absorption at this pH. In the basic medium (pH 6.8), MDT was less than 15 min for G1T, G2A, and M1, whereas the reference was 21.44 min. At pH 4.5, MDT was greater and variable (17.69–41.67 min).

To establish in vitro bioequivalence, the statistical model of the similarity factor (f_2) was used to determine if the obtained dissolution profiles for the generic medicines are similar to the reference (*34*). An f_2 value less than 50 indicates that there are percentage differences between the profiles; a value of 36 indicates a 20% difference, and a value of 41 means a 15% difference. An f_2 value between 50 and 100 indicates that the two profiles are similar, but with some differences; a value of 50 indicates a difference of 10%, 65 means a 5% difference, 83.5 is a 2% difference; and when f_2 is exactly 100, it is concluded that the two dissolution profiles are identical (*5*, *35*). This study found that when compared to the reference, G2A and M1 had differences of 15% at pH 1.2 and more than 20% at pH 6.8. G1T was different from the reference by less than 10% at pH 1.2 and 6.8, and the f_2 values were in the range of 50–100 in both dissolution media (55.42 and 58.75, respectively). Taken together, these parameters (f_2, DE, and MDT) indicate optimal release of risperidone at basic pH in the biopharmaceutical phase; therefore, in vivo, the drug would be absorbed at the intestinal level. However, only one of the three generic medicines (G1T) is considered biopharmaceutically equivalent to the reference brand in both acidic and basic pH.

Our results have an impact on the public health of Peruvians, given that G1T complies with in vitro biopharmaceutical quality controls, which is why it is emerging as a low-cost and accessible alternative for patients with fewer economic resources in the country. This study shows that G1T is an equivalent medication with the reference, ensuring that after release of the API, it is optimally absorbed, reaching plasma levels within the therapeutic range, avoiding therapeutic failure, and minimizing adverse reactions. Additionally, the formulations evaluated in this study are not of dubious origin or falsified.

The results of this study must be considered in the context of various limitations. The main limitation was not comparing the generic products with the innovator drug Risperdal, because it was not available in Peru during the time of the experimental process. Zepidona was used as the reference medication instead according to WHO guidance. Other limitations include having studied only four brands of risperidone tablets out of the eight registered in the country, and not having performed the disintegration test, which are being considered in future studies.

Without prejudice to the above, this research is relevant for generating scientific evidence of the quality of drugs in the in vitro biopharmaceutical release phase, for university researchers to initiate relative bioavailability studies, and for the authorities of the health sector to require in vivo and in vitro bioequivalence studies as a prerequisite for the issuance of the health registry, and for the acquisition of medications by the Ministry of Health of Peru.

CONCLUSION

This study aimed to evaluate the in vitro biopharmaceutical quality of risperidone 2-mg tablets in Lima, Peru and their impact on public health. Only one of three medicines (G1T) was considered biopharmaceutically equivalent to the reference in both acidic and basic dissolution medium (pH 1.2 and 6.8) according to f_2, DE, and MDT.

DISCLOSURES

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