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Original Article

QUALITY EVALUATION OF BRANDS OF PROPRANOLOL HCL TABLETS AVAILABLE ON IRAQI MARKET

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ABSTRACT

Objective: The purpose of this study is to evaluate the quality control of marketed tablets containing propranolol hydrochloride available on the Iraqi market and manufactured by different companies.

Methods: Different batches of propranolol hydrochloride 40 mg tablets were assessed using quality control tests. Weight variation, diameter, thickness, friability, disintegration time and dissolution study were carried out in this study.

Results: Based on the data obtained in this study, all brands of PPL available on the Iraqi market showed weight variation within the acceptable limit of USP. Marketed products of Becardin and Propranolol lie within the acceptable limit of hardness and Inderal was observed to be slightly higher than the normal upper range of USP. Diameter and thickness for all brands were almost the same, except the diameter of Becardin was slightly higher and friability was zero for all brands. All brands demonstrated a time of disintegration of fewer than 30 min. The tested marketed propranolol products; Inderal, Procard, Becardin and Propranolol showed cumulative drug release of 90.08%, 94.46%, 92.4% and 79.51%, respectively at the end of the first 20 min. This variation in the release profile of marketed tablets of Propranolol HCl might be attributed to the excipients present in the marketed tablets where some of these excipients may behave as a disintegrant and enhance dissolution rate while others may act as dissolution retardants.

Conclusion: All marketed tablets of Propranolol HCl employed in this study were produced within the standard criteria of tablet manufacturing. Evaluation of quality control of these selected tablets showed acceptable pharmaceutical properties that lie within the limits of USP.

Keywords: Quality control, Propranolol HCl, Oral tablets

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INTRODUCTION

Quality plays an essential role in the development of pharmaceutical products. Concerning pharmaceutical products, quality may be defined as a product that is free from contaminants and reproducibly gives the pharmacological effect as mentioned in the label [1]. The purpose of pharmaceutical development of a product is to design and establish formulation components and an efficient fabrication process that reliably meets the requirements of quality criteria needed to perform its therapeutic goal. Traditionally, pharmaceutical products are available on the market when the final products are successfully tested. Batches that do not pass the test may influence the sales since they don't possess the needed criteria. Before the manufacturing process, the evaluation of the final product should be achieved in terms of quality criteria. Thus, quality by design (QbD) has been established to provide a product with consistent quality and minimum or no rejected bathes [2].

The quality of raw materials involving additives and drug substances is assessed by testing. If they meet FDA-approved specifications and the proposed manufacturers, they can be invested in the production of the product. With respect to ICH Q8 R2 "A critical quality attribute (CQA) is a physical, chemical, biological, or microbiological property or characteristic that should be within an appropriate limit, range, or distribution to ensure the desired product quality"[3]. CQAs are generally associated with additives, active ingredients, intermediates, and drug products. CQAs of oral solid dosage forms for example, are usually those aspects influencing drug release, product strength, purity and stability, whereas sterility and clarity are linked to the parenteral. The QCAs can also involve properties like bulk density and particle size distribution that have an impact on drug products. For biological/biotechnological products, CQA_S of drug products are mostly linked with the drug material. Impurities represent an important aspect of potential drug material CQA_S. Dissolution test is essential for a drug product with a controlled release, whereas for drug products with an immediate release, it will not show a critical attribute for the quality control concept [4, 5].

The oral drug delivery system considers the most convenient route for drug administration of therapeutic agents because of ease of administration, lower cost, and high patient compliance in comparison to the parenteral route [6]. Propranolol HCl, a beta-adrenoceptor blocker, is used as an antianginal, antiarrhythmic and antihypertensive agent. It has a short half-life (3-4h) and undergoes extensive first-pass metabolism by the liver, where about only 25% of the drug is delivered to the systemic circulation [7]. Tablets are usually manufactured using pharmaceutical additives. They may differ in shape, weight, size, thickness, hardness, disintegration, and release behaviour, based on their method of manufacturing and purpose of use [8]. Propranolol HCl is available on the market as an oral tablet solid dosage form for the treatment of angina, hypertension and arrhythmia. In Iraqi markets, Propranolol HCl tablets are available and manufactured by different pharmaceutical companies that carry standards of pharmacopeia.

MATERIALS AND METHODS

Materials

Propranolol HCl (PPL) powder was obtained from Zhejiang Menovo Pharmaceutical Co, LTD. Hydrochloric acid (HCl) was ordered from Thomas Baker, India.. Marketed products of propranolol 40 mg film-coated tablets used in this study were obtained from private pharmacies in Kufa, Iraq, and are illustrated in table 1.

Methods

Determination of melting point

A capillary glass tube was used for the determination of the melting point of PPL. A small amount of powder is placed into the tube that is opened from one end and sealed from another end. The tube was then inserted into a digital melting point apparatus. When the

melting of the powdered drug is completed, the melting temperature is recorded [9].

Table 1: Marketed products of propranolol HCl 40 mg tablets used in this study

Trade name	Company	Country
Inderal	AstraZeneca	UK
Procard	Pioneer	Iraq
Propranolol	Accord	UK
Becardin	SDI	Iraq

UV-Vis spectroscopy

The calibration curve of PPL was obtained using UV-Vis spectroscopy by plotting the concentration of the drug-using stock solution of PPL against the absorbance. A standard solution of PPL was prepared by dissolving PPL in 0.1N HCl over a range of concentrations (5-50 µg/ml). A serial dilution was used to prepare different concentrations of stock solution of PPL. The absorbance of PPL solution was determined at 295 nm utilising a quartz cuvette of 10 mm in a UV spectrometer (UV 1800 Shimadzu). The correlation coefficient (R^2) was used in determining the linearity of the regression.

Weight variation test

In this test, 20 tablets of PPL were selected randomly from different companies. These tablets were weighed individually. Weight variation was determined using the following equation:

$$\frac{(\text{Individual weight} - \text{Average weight})}{\text{Average weight}} * 100 \text{ .... Equation 1}$$

The sample meets the standards if the individuals don't differ from the mean by more than is accepted in terms of percentage. That means if no more than two tablets exceed the percentage limits and if no tablet varies by more than two times the accepted limit in terms of percentage, the tablets will meet the USP weight variation tests (table 2) [10].

Table 2: USP weight variation test

Average weight of tablet (mg)	Maximum (%) weight difference allowed
130 or less	10
130-324	7.5
More than 324	5

Friability test

A friabilator was used to evaluate the friability and to assess the tendency of the tablet to chip, crumble or break upon handling or compression as well as the strength of the tablet. A preweighed tablet sample is placed in the friabilator (Erweka friabilator tester). The friabilator was operated at 100 rpm. The weight of the tablet was assessed before and after a specified number of revolutions so the weight loss can be evaluated. Tablets can pass the friability test if the percentage of weight loss is within the range of 0.5%-1% of tablet weight. The percent friability can be determined using the following equation [11]:

$$\% \text{ friability} = \frac{I-F}{I} * 100 \text{ .... Equation 2}$$

Where I represents initial weight and F denotes weight after friability.

Hardness test

The force required to diametrically break a tablet can be defined as hardness which represents a crushing strength of a tablet. The crushing strength of a tablet can be evaluated using Erweka hardness tester. From each brand, a ten tablets sample was tested and the pressure required to break the tablet was recorded as kg/cm^2 [12].

Determination of tablet thickness and diameter

10 tablets from each brand were taken and both the thickness and diameter of the tablets were determined using Erweka hardness tester. The mean and standard deviation, were calculated for each brand [12].

Disintegration test

The disintegration time of the tablet was assessed by using a USP disintegration apparatus (Erweka, Germany); the apparatus is composed of 6 tubes open at both ends where the bottom of the tube is composed of a 10-mesh screen. The medium was simulated body fluid and the temperature was kept at 37±2 °C. The disintegration time was determined when the complete disintegration of the tablet occurred.

Drug release study

The quality of marketed propranolol tablets was assessed using dissolution experiments carried out on marketed tablets fabricated by different companies. USP Apparatus 1 (basket) was used to study the *In vitro* drug release study. The temperature was adjusted at 37.0±0.5 °C and the rotation of the paddle was at 100 rpm. Branded tablets of different companies were placed in 900 ml (0.1N HCl). An aliquot of 5 ml of release medium was withdrawn at predetermined time intervals (5, 10, 15, 20, 25, 30, 35 and 45 min) and substituted with an equal volume of fresh medium to maintain a constant volume. These aliquots of release medium were filtered through a 0.45µm cellulose acetate membrane filter unit before analysis. Analysis of samples was then performed using a Cary 50 UV-Visible spectrophotometer at 295 nm.

RESULTS AND DISCUSSION

Measurement of melting point

The melting point of PPL was determined to be 163 °C to 164 °C [13]. This represents a purity indicator of powdered PPL used in this study

Calibration curve of PPL

The absorbance was plotted against the diluted concentrations of stock solution of PPL to construct the calibration curve. Absorbance measurements over the range of concentrations were observed to be linear with a high value of correlation coefficient (R^2) (fig. 1).

Weight variation test

Based on the USP, the acceptable limit of weight difference of tablet is±7.5 for a tablet weighing more than 130 mg as mentioned in table 2. The results obtained from the assessment of weight variation demonstrated that all brands of PPL available on the Iraqi market showed weight variation within the acceptable limit of USP. Table 3 illustrates the data of the weight variation test of PPL.

Friability test

Evaluation of friability was carried out in triplicate for each brand of PPL oral tablets. All brands revealed no percent loss after reweighing the tablet so the value of friability for all brands was zero. This could be related to the nature of marketed tablets which are film-coated where there is no abrasion during friability test [14].

Hardness test

To resist the mechanical strength of processing, manufacturing, and transportation, a tablet should possess a minimum strength which is defined as its hardness. Concerning USP, a crushing force of 4-8 Kg is acceptable for an uncoated tablets [15]. The results of hardness evaluation showed that marketed products represented by Becardin and Propranolol lie within the acceptable limit of hardness and Inderal was found to be slightly higher than the upper normal range. On the other hand, Procard was exceeding the normal limit of hardness (table 4). This might be related to the effect of compression on the particle bonding, where a high compression force may retard tablet wettability and consequently, an increase in the hardness and density of the tablet may occur [16].

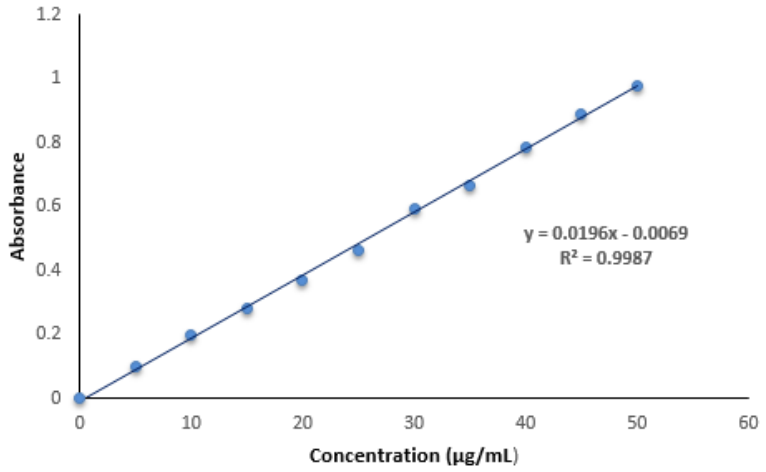

Fig. 1: Calibration curve of propranolol (pH 1.2) (n=3)

Table 3: Data for weight variation test of PPL tablets

Tablet No.	Weight of individual tablet (IW) (mg)				% Deviation (IW-Aver)/Aver *100			
	Inderal	Procard	Becardin	Propranolol	Inderal	Procard	Becardin	Propranolol
1	208.3	207.1	261.1	197.5	0.64	1.29	-0.88	2.60
2	205.1	206.7	261.4	192.4	-0.90	1.09	-0.76	-0.05
3	203.1	201.7	263.1	192.9	-1.87	-1.35	-0.12	0.21
4	204.4	206.8	265.4	193.8	-1.24	1.14	0.76	0.68
5	208.3	200.9	266	195.7	0.64	-1.75	0.98	1.67
6	206	205.7	257.8	193	-0.47	0.60	-2.13	0.26
7	209.3	207.8	261.2	193.7	1.13	1.63	-0.84	0.63
8	205.2	204.2	261	189.3	-0.86	-0.13	-0.91	-1.66
9	209.3	203.7	261.9	189.7	1.13	-0.38	-0.57	-1.45
10	210.5	206	267	193.7	1.71	0.75	1.36	0.63
11	205.9	206.4	263.8	192.5	-0.52	0.94	0.15	0.01
12	207.8	202.2	258.7	195.5	0.40	-1.11	-1.79	1.56
13	207.3	203	266.4	193.6	0.16	-0.72	1.14	0.58
14	204	206	261.6	193	-1.43	0.75	-0.69	0.26
15	206.1	204.1	264.5	188.5	-0.42	-0.18	0.41	-2.07
16	210.5	205.2	268.8	192.9	1.71	0.36	2.05	0.21
17	203.9	201.2	263.6	190.8	-1.48	-1.60	0.07	-0.88
18	209.3	207	264.5	190.1	1.13	1.24	0.41	-1.24
19	207.9	204.6	267.3	191.4	0.45	0.06	1.48	-0.57
20	207.2	199.1	263.1	189.8	0.11	-2.63	-0.12	-1.40
Mean	206.97	204.47	263.41	192.49				
SD	2.25	2.44	2.89	2.32				

Data are represented as (mean±SD, n = 3).

Friability test

Evaluation of friability was carried out in triplicate for each brand of PPL oral tablets. All brands revealed no percent loss after reweighing the tablet so the value of friability for all brands was zero. This could be related to the nature of marketed tablets which are film coated where there is no abrasion during friability test [14].

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Tablet thickness and diameter

Thickness and diameter measurements are measured because of their influence on packaging as well, as they can be employed in the determination of tablet tensile strength [17, 18]. The results showed that thickness and diameter for all brands were almost the same, except the diameter of Becardin was slightly higher as indicated in table 4.

Disintegration time

Disintegration time plays an essential role in the assessment of quality control of oral tablets intended for immediate release tablets that can be used in the treatment of chronic diseases like heart failure and hypertension where a rapid onset of action is needed. Regarding USP, the maximum time of uncoated tablet disintegration is 30 min [19]. Based on the results, all brands demonstrated a time of disintegration of less than 30 min (table 4). Variation in disintegration time was noticed among all brands, where disintegration time was short for Becardin, 1.13±0.22 min, while for propranolol was slow 8.40±0.70 min. This variation in disintegration time may be related to the presence of disintegrants variably in the tablet. Concerning Inderal and Procard, the time of disintegration

was not affected by the high value of hardness. In a study conducted by Conceição AP *et al.* (2018), the dissolution profiles of 40-mg tablets of propranolol available as a reference, generic and similar drug products sold commercially in Bahia, Brazil were studied. It was observed that there were differences in disintegration times between the reference drug and the generic and similar drugs. Authors attributed these differences to the presence of different excipients in the formulations. Generic and similar products contain a greater amount of excipients with disintegrating functions in comparison to those in the reference drug [20].

Table 4: Thickness, diameter, hardness, friability and disintegration time of PPL tablets

Brand	Thickness (mm)#	Mean diameter (mm)	Hardness (Kg/cm²)#	Friability (%)	Disintegration time (second)#
Inderal	3.455±0.018	8.57	8.33±0.54	0	3.07±0.36
Procard	3.764±0.018	8.24	12.59±1.12	0	2.92±0.20
Becardin	3.908±0.019	9.10	5.33±0.30	0	1.13±0.22
Propranolol	3.474±0.021	8.05	7.48±0.42	0	8.40±0.70

#Data are represented as (mean±SD, n = 3).

Dissolution behaviour of marketed PPL tables

Cumulative % drug release patterns of PPL in marketed products were plotted against time. Fig. 2 demonstrates the release profiles of Inderal, Procard, Becardin and Propranolol. All conventional tablets of PPL revealed cumulative % release of more than 80% within 15 min. Propranolol and Inderal exhibited a cumulative release of 19% and 47% within 5 min, respectively. On the other hand, Procard and Becardin demonstrated a cumulative release of more than 92% within 5 min. This variation in release behaviour of PPL from these commercial tablets may be attributed to the excipients contained in the tablets where some of these excipients may act a disintegrants and enhance dissolution rate while others may act as dissolution retardants for example, lubricants in high amounts [20, 21]. *In vitro* comparative dissolution profiles of different propranolol, generic tablets available in Bangladesh were studied. Shuma ML *et al.* (2021) have tested four different products of propranolol 10 mg tablets. All four local products had a suitable dissolution pattern with the reference brand (at least 80% of the propranolol was dissolved in the medium after 30 min) [22].

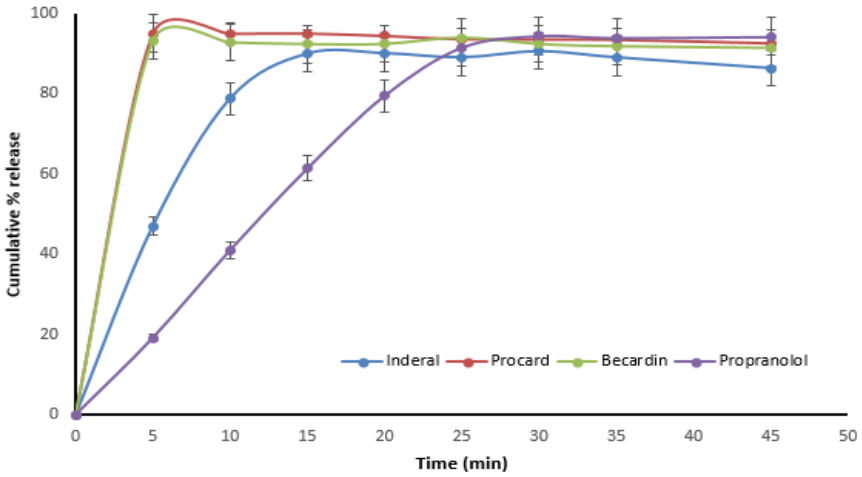

Fig. 2: Drug release profiles of PPL tablets manufactured by different companies as a function of time in pH1.2. Error bars indicate the standard deviation of replicates (n=3)

CONCLUSION

Marketed products of PPL available on the Iraqi market were evaluated using quality control tests represented by weight variation, friability, thickness, diameter and hardness. Disintegration time, as well as dissolution behaviour, were determined. Concerning quality control tests, the results revealed that all marketed products tested meet the pharmacopeia limit. The disintegration time of all brands was less than 30 min and the cumulative % release was more than 80% within 15 min.

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AUTHORS CONTRIBUTIONS

All the authors have contributed equally.

CONFLICT OF INTERESTS

Declared none

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