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# Quality assessment of selected marketed irbesartan 300mg tablets brands in Iraq

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**Abstract**
**Objective:** The goal of this study was to assess the quality of some selected irbesartan products in community pharmacies in Iraq.
**Methods:** Different parameters of quality control of pharmaceutical products can guarantee the quality and bioavailability and optimal therapeutic activity. Used quality control parameters, i.e., the variation of weight, friability, content uniformity, disintegration time and dissolution profiles were assessed *in vitro*.
**Results:** The weight range of Aprovel 300mg was in range of 0.505 g-0.523g while Converium weight range of 0.594-603 g and Gizlan 300 mg weight range was of 0.495-0.507g.
**Conclusion:** The results showed that all products fulfill the given specification of Pharmacopeia (USP-NF) except Converium which its dissolution rate was less than % in USP (80% after 20 min).

**Keywords:** irbesartan, quality control evaluation, hardness, dissolution

## Introduction

Irbesartan is designated chemically as 1,3- diazaspiro [4.4]non-1-en-4-one, 2 – butyl -3- [[2´-(*1H*-tetrazol-5-yl) [1,1´-biphenyl]- 4-yl]methyl]-.2 Butyl-3-[*p*-(*o*-1*H* -tetrazol-5-ylphenyl) benzyl]-1,3- diazaspiro[4.4]-non-1-en-one. It has molecular formula $C_{25}H_{28}N_6O$, molecular weight 428.53 [1] and it has structural formula:

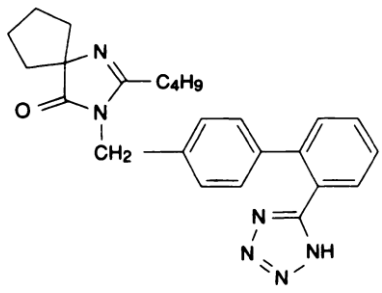


**Fig 1**

Irbesartan is white to off white crystals powder, Crystals from ethanol 96%, mp 180-181ºC. Slightly soluble in alcohol and methylene chloride, it is practically insoluble in water. Its partition coefficient log p (octanol/water) 10.1 [2, 3]. In 1997, the FDA granted approval of irbesartan to the market for treatment of hypertension [4].

Irbesartan is a specific antagonist of angiotensin II receptors ($AT_1$ subtype) where Angiotensin II is an important component of the renin-angiotensin system and is involved in the pathophysiology of hypertension and in sodium homeostasis. Irbesartan does not require metabolic activation for its activity. Irbesartan blocks the potent vasoconstrictor and Aldosterone-secreting effects of angiotensin II by selective antagonism of the angiotensin II ($AT_1$ subtype) receptors localized on vascular smooth muscle cells and in the adrenal cortex. It has no agonist activity at the $AT_1$ receptor and a much greater affinity (more than 8500-fold) for the $AT_1$ receptor than for the $AT_2$ receptor (a receptor that has not been shown to be associated with cardiovascular homeostasis) [5].

## Materials and Methods

### Materials

Hydrochloric acid was supplied by Ibn Hayyan University College, Karbala, Iraq.

### Marketed Products

Aprovel 300mg tablets, Sanofi, France, Lot: 5A44, manufacture date: 08-15, expire date: 07-18. Converium 300mg tablets, Medochemie, Cyprus, lot: E9F066, Manufacture date: 12-2015, expire date: 12-2018 and Gizlan 300mg tablets, Dar aldawa, Jordan, lot: 56bb, manufacture date: 03-17 and expire date: 03-20.

### Analytical Method

Accurately weighed irbesartan was dissolved in 0.1 N HCl in a 100 ml volumetric flask. From the stock solution, different dilutions were prepared to generate a calibration curve by measuring absorbance using UV spectrophotometer (UV-Spectrophotometer AVI-2700, labtech, Ined) from 200-400 nm. The concentration of irbesartan was calculated using the linear regression equation of the calibration curve. Mean standard error and RSD (precision) calculated in the study were 0.003% and 0.74% respectively, (n = 6).

### Construction of calibration curve in 0.1 N HCL

A weight of irbesartan was accurately weighed (equivalent to 300 mg irbesartan) and transferred into 100 ml volumetric flask, 2 ml methanol was added and shaken for 5 min to dissolve, completed to the volume using 0.1 N HCl, mixed well then diluted to give serial concentrations of irbesartan in the range of µg/ml in 0.1 N HCl, filtered, scanned in the range of 200-400 nm (UV system in the range of 200-400 nm with 1 cm matched quartz cells) using 0.1 N HCl as a blank and λ 246 nm was chosen to be the maximum $\lambda_{max}$ and the calibration curve was constructed [3].

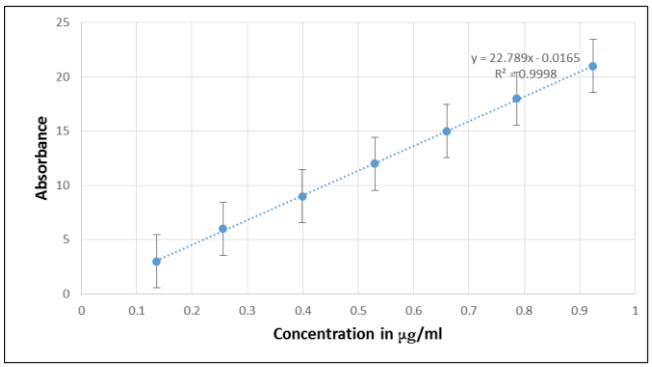


**Fig 2:** Graph representing calibration curve of irbesartan in HCl. Error bars represent standard deviation of the mean (±standard deviation)

**Evaluation tests for the selected products**

**Weight variation**

For each brand, ten tablets were randomly selected and weighed individually using an analytical balance (Electronic balance, China). The average weights were determined and the percentage deviations from mean values were calculated. Then the standard deviation, and percentage of related standard deviation (RSD) was determined [2].

**Assay**

The quantity of irbesartan was determined in each product according to USP 30. 10 tablets were weighed and average weight was found out, a weight equivalent to 100 mg of irbesartan was transferred into 100 ml volumetric flask, 5 ml of methanol. Serial dilution was done and measure at 246 nm with the UV spectrophotometer. The amount of irbesartan in each product was calculated using the equation of the calibration curve.

**Hardness test**

Tablet hardness is defined as the force required breaking the tablet in a diametric compression test. If the tablet is too hard, it may not disintegrate in the required period of time to comply with the dissolution specification. Conversely, the hardness must not be so low that the tablets are soft and friable. To get a satisfactory quality tablet hardness should be between 4 and 8 kg 6. The results of the branded products (Table 2) for the hardness test were satisfactory type hardness tester (YD-2/ Guoming, China).

**Disintegration time test**

The disintegration is used as a guide to the formulator in the preparation of a satisfactory tablet formula as a control test on the process. Therefore, to ensure batch-to-batch product uniformity, DT test is very important.

USP-35 disintegration apparatus (ElBJ-, Guoming, China) containing 6 glass tubes that are 3 inches long, open at the top and are held against a 10-mesh screen in the lower end of the unit basket rack was used in the study. For the test, a tablet was placed in each tube and the frame of the basket was placed in a beaker containing 1 liter of distilled water to $37^0$C, such that the tablets remain below 2.5 cm the surface of the media in its upward movement and descent no closer than 2.5 cm from the bottom of the beaker. In the apparatus, a standard motor driven device is set for moving the basket containing the tablets upwards and downwards through a distance of 5.3 to 5.7 cm at a frequency of 29 to 32 cycles per minute. The disintegration time of each tablet was determined and the average time was calculated [1].

**Content uniformity**

The uniformity of content was determined by crushing ten tablets from each formula and determining the drug content of each tablet individually using the developed method [6].

***In vitro* dissolution rate studies**

The dissolution studies were carried out according to the USP paddle method. The stirring rate was 50 rpm at 37 ± 0.5 °C. The dissolution medium was 1000 ml of 0.1 M HCl [2]. The samples (n= 12) were at ten minute intervals withdrawn at 5, 10, 15, 20 and 30 minutes and assayed spectrophotometrically at 246 nm. The percentage of cumulative drug release of each tablet was determined using the linear regression equation of the calibration curve.

**Comparison of dissolution profiles**

As a model independent approach, here, one adjustment factor (f2) comparing the dissolution profile of a pair of pharmaceutical products were applied to the dissolution data; f2 value between 50 and 100 were used to define the equivalence of two dissolution profiles.

$$f2 = 50.\ log\ \{[1 + (1/n).\ St = 1^n\ (Rt - Tt)^2]^{-0.5}.\ 100\}$$

Where, n is the number of dissolution sample times, and Rt and Tt are the mean percent dissolved at each time point t for the reference and test dissolution profiles respectively.

**Results and Discussion**

The weight range of Aprovel 300mg was in range of 0.505 g-0.523g with standard deviation 0.004 while converium weight range of 0.594-603 g with standard deviation 0.003 and Gizlan 300 mg weight range was of 0.495-0.507 g with standard deviation 0.004. The results are shown below in table 1 and 2.

**Table 1:** Weight variation Measurement (n = 10)

| | Aprovel | Converium | Gizlan |
|---|---|---|---|
| | 0.505 | 0.598 | 0.495 |
| | 0.516 | 0.601 | 0.502 |
| | 0.510 | 0.603 | 0.505 |
| | 0.506 | 0.594 | 0.507 |
| | 0.507 | 0.601 | 0.506 |
| | 0.506 | 0.601 | 0.506 |
| | 0.510 | 0.603 | 0.505 |
| | 0.511 | 0.594 | 0.507 |
| | 0.512 | 0.601 | 0.506 |
| | 0.513 | 0.601 | 0.506 |
| Mean (g) | 0.510 | 0.600 | 0.505 |
| Minimum | 0.503 | 0.594 | 0.495 |
| maximum | 0.516 | 0.603 | 0.507 |
| Standard deviation (SD) | 0.004 | 0.003 | 0.004 |

The hardness mean of Aprovel 300mg was 20.4 kg/cm3 with standard deviation 0.01 while converium hardness was 10 kg/cm3 with standard deviation of 0.06 and Gizlan 300 mg weight range was of 20.4 kg/cm3 standard deviation 0.12

**Table 2:** Results of quality tests

| Brands | Hardness* kg/cm3 **(mean ± SD)** | Assay* **(%)** | Content uniformity* **(%)** | Disintegration time* **(min)** | Average drug release after 20 min* **(%)** | Similarity factor |
|---|---|---|---|---|---|---|
| **Aprovel** | 20.4± 0.01 | 101%± 0.2 | 99%± 0.4 | 11%± 0.05 | 92 ± 0.6 | |
| **Converium** | 10± 0.02 | 98%± 0.3 | 97%± 0.1 | 0.5%± 0.08 | 75± 0.8 | 39 |
| **Gizlan** | 20.4± 0.05 | 98.5%± 0.2 | 96.9%± 0.2 | 10.5%± 0.1 | 90± 0.2 | 73 |

*All values are reported as mean ± standard deviation (SD), n=6.

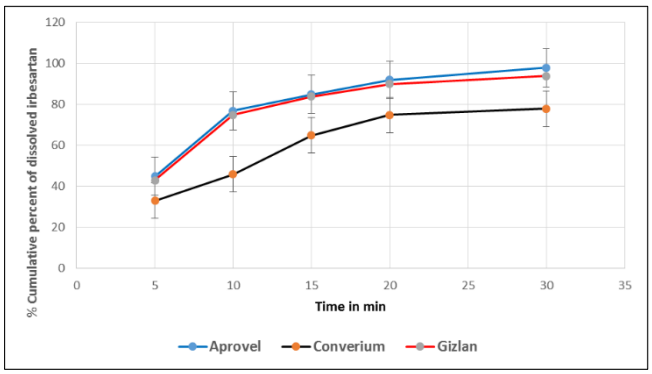


**Fig 3:** Dissolution profile of irbesartan from prepared tablets (values represent mean ±SD, n=6)

## Conclusion

From the study it was identified that weight variation, assay, disintegration time, content uniformity and hardness of irbesartan tablet brands complied the specification. Finally, as quality control parameters complied to USP except for Converium which its dissolution rate was less than % in USP (80% after 20 min) [1] also dissolution profile was not similar to Aprovel as reference product.

## Author's contribution

There is one author only who performed all procedures, tests and write the manuscript.

## Conflicts of interest

The author declares there is no conflict of interest.

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