Univesity Of Basrah

College Of Pharmacy

- **Evaluation of different physicochemical properties of different marketed products from different companies (parallel import products)**

This project is submitted to the department of pharmaceutics as a partial fulfilment for graduation in college of pharmacy

By:

Abdulmohsen Faisal Ghazi

Rasoul Raheem Mazeal

Zahraa Arkan Abdulamir

(5th stage)

Supervised by:

Dr. Ahmed Abdulkareem

2022-2023

1. Abstract

Rosuvastatin is a HMG-CoA reductase inhibitor (Statin) which inhibit the rate limiting step in cholesterol biosynthesis. it possess lipid lowering effect and used to prevent cardiovascular disease and treat dyslipidemia and it is widely marketed in the Republic of Iraq.

The study aims to evaluate the in vitro quality of four rosuvastatin film coated tablets 20mg formulations that are commercially most commonly used in the Republic of Iraq markets.

rosuvastatin tablets were tested include non-pharmacopoeia (non-official) tests like organoleptic properties, friability,thickness, and hardness, and some pharmacopoeia (official) tests according to USP like weight variation, disintegration time, dissolution, and content uniformity

Our data indicated that the rosuvastatin tablet investigated in our study meets the in vitro quality control of the official specifications, is chemically equivalent, and does not vary in physiochemical qualities.

2. Introduction

Tablets are solid dosage forms usually prepared with the aid of suitable pharmaceutical excipients. They may vary in size, shape, weight, hardness, thickness, disintegration, and dissolution characteristics and in other aspects, depending on their intended use and method of manufacture. Most tablets are used in the oral administration of drugs. Many of these are prepared with colorants and coatings of various types. Other tablets, such as those administered sublingually, buccally, or vaginally, are prepared to have features most applicable to their particular route of administration. Tablets are prepared primarily by compression, with a limited number prepared by molding. Compressed tablets are manufactured with tablet machines capable of exerting great pressure in compacting the powdered or granulated material. Tablets are said to be most widely used conventional dosage forms due to its variety of advantages and 70% of the medicaments were dispensed in tablet forms.

2.1 Classification of tablets dosage form:

• Tablets are classified according to their route of administration. The following are the four main classification groups**:-**

A.Tablets ingested orally**:**

Ex: 1-Sugar coated tablets**.**

2-Film coated tablets**.**

C. Tablets administered by other routes**:**

Ex: 1. Implantation tablets**.**

2. Vaginal tablets**.**

B. Tablets used in the oral cavity**:**

Ex: 1. Sublingual tablets**.**

2. Buccal tablets**.**

Tablets used to prepare solutions**:**

Ex: 1. Effervescent tablets**.**

2. Dispensing tablets**.**

2.2 Advantages:

• <u>Production aspect</u>

– Lowest cost production

– Easiest and cheapest to package and ship

– High stability

• User aspect (doctor , pharmacist and patient)

– Easy to handling

– Accurate dosing

– Ease of Administration

– Coating can mask unpleasant tastes & improve patient acceptability

2.3 Disadvantages:

- Administration of drugs is not easy in case of children.
- Individualized Dosing: Tablets often come in fixed strengths, which may not always align with an individual's specific dosage requirements. This can result in the need for multiple tablets or the need to break or cut tablets, which can be inconvenient or impractical.
- Special Coating Requirements: Certain medications may require specific coatings or formulations to protect the active ingredient or enhance drug release characteristics. This may increase manufacturing complexity and costs.
- Hygroscopic nature of drugs is unacceptable for tablet compression.

2.4 Evaluation:

The evaluation of tablets is done using a number of tests which can be classified into:

2.4.1 The official tests like:

- ✓ **Weight Variation Test**

The weight variation test of tablet are used to confirm the tablet has the required amount of active drug.

Limits according to U.S.P:

Average mass of tablets	% of deviation
<80 mg	±10.0
80 -250 mg	±7.5
>250 mg	±5.0

✓ **Content Uniformity Test**

Determines the amount of drug in a sample of tablets. For tablets in which the active ingredients make up about 90% of the tablet weight, the weight variation test will give a good measure of content uniformity.

❑ The acceptable potency range for low-dose, highly potent drugs is 90%-110%.

❑ For large-dose drugs, the range is 95%-105% of the labelled amount.

❑ No tablet should fall in the range of 75 – 125% deviation (tablets then classified as under-doses or over-dosed).

✓ **Disintegration Test**

• Disintegration measures the time that is required for a tablet to break up into a small particles at certain conditions (temp, media).

• Disintegration test is indicated for all tablets except :

•Chewable tablets

•those tablet should dissolve slowly such as lozenges, glycerine trinitrate

•some types of sustained release products

✓ **Dissolution**

• This test determines the amount of active ingredient(s) released from a solid oral dosage form (tablet) under controlled conditions using a known volume of dissolution medium within a predetermined length of time.

2.4.2 The non-official tests like:

- **General Inspection**

❑ visual examination and physical evaluation of the tablet's appearance, size, shape, color, and overall quality. These tests are typically performed during the manufacturing and quality control processes to ensure that the tablets meet the required standards and specifications.

I) ORGANOLEPTIC PROPERTIES

▸ (colour, presence or absence of odour is important for consumer acceptance, taste, surface texture and consistency)

▸ The color of a product must be uniform within a single tablete.

II) SIZE & SHAPE

Measured by :-

- ❖ Micrometer
- ❖ Sliding calliper scale

Tablet thickness should be controlled within +5% variation of standard value.

- ✓ **Hardness Test**

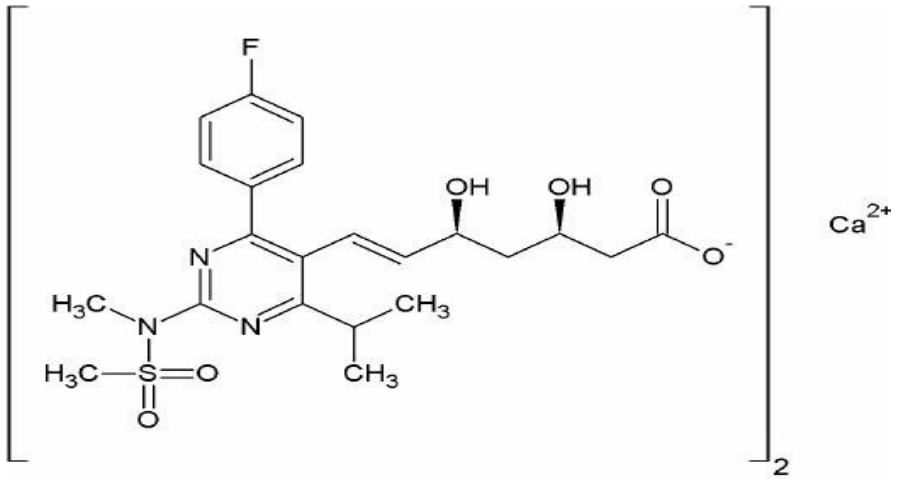
Hardness is generally expressed as the force required to break a tablet in a diametric compression test; it is often called breaking strength or tablet crushing strength

- ✓ **Friability Test**

❑ Friability is a measure of the tendency of a tablet to powder, chip, and fragment during handling and is another measure of tablet strength.

❑ friabilator (friability tester) is used to measure the friability of a tablet.

-Rosuvastatin is a medication belonging to the class of drugs known as statins. used to lower lipid levels and reduce the risk of cardiovascular disease including myocardial infarction and stroke. Rosuvastatin exerts its therapeutic effects by inhibiting the enzyme called HMG-CoA reductase, which plays a crucial role in cholesterol synthesis in the liver. By inhibiting this enzyme, rosuvastatin reduces the production of cholesterol, resulting in decreased levels of LDL It is also modestly increases HDL .



-Rosuvastatin belongs to the class of organic compounds known as phenylpyrimidines. These are polycyclic aromatic compounds containing a benzene ring linked to a pyrimidine ring through a CC or CN bond. Pyrimidine is a 6-membered ring consisting of four carbon atoms and two nitrogen centers at the 1- and 3- ring positions..

-<u>The Chemical Formula</u>

$C_{22}H_{28}FN_3O_6S$

-<u>Molecular Weight</u>

481.5 g/mol

3. Experimental work:

3.1 Materials:

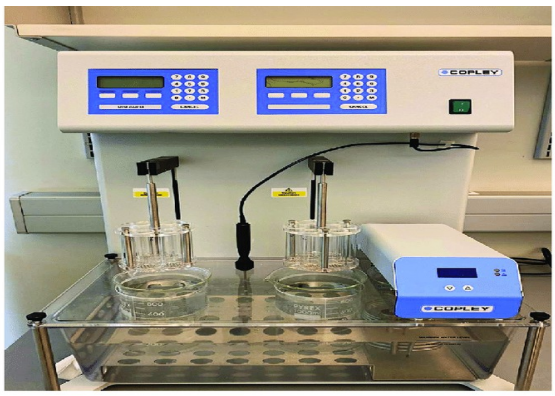
- Film coated rosuvastatin tablets 20mg of four different companies coded as (A, B, C, and D). ¬ Ethanol 99.99% ¬ Distilled water.
- Phosphate buffer.

3.2 Equipment's:

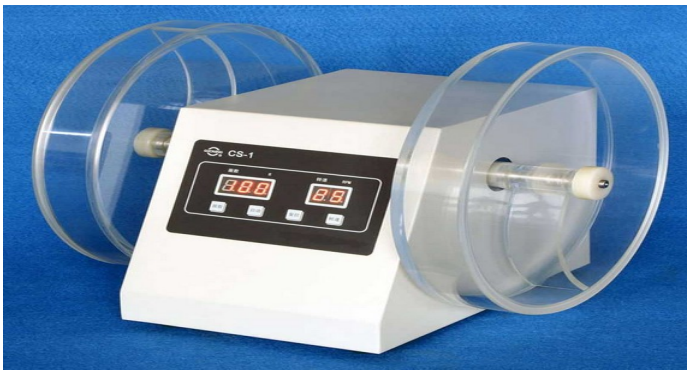
Sensitive balance (G&G), UV-visible spectrophotometer (Cecil), disintegration apparatus (Copley), double dram friabilator (Copley) , hardness tester (ERWEKA), Digital calliper (Copley), dissolution apparatus.

Sensitive digital balance

UV-visible spectrophotometer



Disintegration tester



Friability tester

Hardness tester

Caliva dissolution tester

Thickness tester (Digital calliper)

3.3 Methods: Official Tests

- **Weight Variation Test:**

Twenty tablets were taken randomly of each company and measure the weight of each tablet individually. Then measure the average mass.

Individual weights are compared with the average weight.

1. If 1 tablets is out of the range, but less than double the allowed % (pass)
2. If 2 tablets is out of the range but less than double the allowed % (pass)
3. If 3 tablets deviate more than the allowed range % (failed).

4. If only one deviate more than the double allowed limit (failed)

- **Content Uniformity Test:**

Select randomly a 10 tablets-sample of each company, then examine each tablet individually, grind it and transfer into 100 ml volumetric flask. Then dissolve in 100ml (99.99%) ethanol and filter the resultant solution.

Dilute 1 ml of filtrate in Suitable volume of ethanol and measure the absorbance of the resulting solution .Use the calibration curve to calculate the recovered concentration of rosuvastatin and use dilution factor to calculate the amount of active ingredients in each tablet. Finally compare the recovered amount of active ingredient the allowed deviation percentage which stated in USP. (The allowed percentage is ±15% of the stated potency).

- **Disintegration Test:**

We use the U.S.P. device (disintegrator) uses 6 glass tubes that are 3 inches long.

To test for disintegration time, take 6 tablets randomly from 18 tablets of each company, Place one tablet in each of the six tubes of the basket at 37c

• Start the apparatus (to move the basket assembly containing the tablets), and record the time required for all of the six tablets to break into particles and to pass to the disintegration medium.

Dissolution Test:

This test aims to quantify the active ingredient(s) released from a solid oral dosage form using specific controlled conditions. The conditions involve maintaining a temperature of approximately 37°C and stirring the solution at a speed of 50rpm in a phosphate buffer with a volume of 900ml and a pH of 5.8.

To perform the test, one tablet from each company is placed individually in separate jars within a dissolution tester. The dissolution apparatus is then initiated, running for

a duration of 30 minutes. After the allotted time, a sample is withdrawn from each jar and subsequently filtered. The filtered samples are subjected to analysis using a UV spectrophotometer, which measures the absorption of UV light at the wavelength where the active ingredient exhibits maximum absorbance, typically around 264 nm. The concentration of the active ingredient is determined by applying a calibration curve to the obtained absorbance values.

Tolerance: not less than 80% of the labelled amount of rosuvastatin is dissolved in 30 min.

Non-Official Tests

- **General Inspection:**

❑ Visual inspection and identification for any flaws that may affect the appearance.

- **Hardness Test:**

❑ In this test, six tablets are positioned individually between two anvils. Force is exerted onto the anvils using a hardness tester, and the amount of force required to fracture the tablet is measured and recorded as the crushing strength. The crushing strength is typically reported in kilograms (kg). This test provides valuable information about the mechanical strength and integrity of the tablets.

❑ Tablet hardness should be between 6 – 10 kg.

- **Thickness Test:**

Twenty tablets were taken randomly of each company and measure the diameter and thickness of each tablet individually with a digital calliper and then obtain the average diameter and thickness and percentage of deviation. Thickness and diameter should be within ± 5% variation of a standard value.

- **Friability test:**

For this test, a random selection of 20 tablets is chosen, and their weights are measured using a precise digital balance. The tablets are placed inside a friabilator and rotated for a duration of 4 minutes, to approximately 100 rotations. After completion, the tablets are carefully removed from the machine. Then the tablets are re-weighed using the balance. To calculate the weight loss percentage, the following friability test equation is applied, taking into account the difference in weights before and after the test:

Weight loss % = [(Initial weight - Final weight) / Initial weight] × 100

Friability Limits: It should be not more than 1.0%.

4. Results and discussion:

In our study, rosuvastatin 20 mg of four different companies (A, B, C, and D) have been evaluated through officials and non-officials test. This test performed by use standard equipment's and prescribed methods, the following results have been obtained:

4.1 officials test:

4.1.1 Weight variation test:

The purpose of this test is to make sure that the entire tablets under observation have uniformity in weight and have the required amount of labelled drug.

The acceptable range of weight variation for ibuprofen 400mg tablets should follow deviation %=5%.

The weight of twenty ibuprofen tablets of each companies were measured as well as the standard of deviation. The results are listed in the table:

No.	A (Tablet wt. (Tablet wt. in g)	B (Tablet wt. in g)	C (Tablet wt. in g)	D

Tab 1	0.20	0.23	0.24	0.25
Tab 2	0.21	0.23	0.25	0.26
Tab 3	0.22	0.23	0.24	0.25
Tab 4	0.22	0.23	0.25	0.24
Tab 5	0.21	0.22	0.25	0.24
Tab 6	0.21	0.22	0.24	0.27
Tab 7	0.22	0.22	0.24	0.24
Tab 8	0.21	0.23	0.24	0.25
Tab 9	0.20	0.23	0.24	0.23
Tab 10	0.21	0.23	0.24	0.24
Tab 11	0.21	0.22	0.23	0.27
Tab 12	0.22	0.22	0.24	0.26
Tab 13	0.21	0.23	0.25	0.24
Tab 14	0.22	0.22	0.23	0.23
Tab 15	0.21	0.22	0.25	0.26
Tab 16	0.21	0.23	0.23	0.26
Tab 17	0.20	0.22	0.24	0.24
Tab 18	0.22	0.23	0.25	0.24
Tab 19	0.21	0.23	0.25	0.25
Tab 20	0.21	0.22	0.24	0.23
Av.wt	0.222.5	0.225	0.2305	0.2475
Accepted Range (+/-7.5%)	222.5-16.5 mg 222.5+0.16.5mg	225-16.87mg 225+16.87mg	230.5-17.28mg 230.5+17.28mg	247.5-18.56mg 247.5+18.56mg

The results indicate all tablets of each company are complying with USP weight limits.

4.1.2 Content uniformity test:

This test performed to ensure that every tablet contains the same amount of drug substance with a defined allowed variation within a batch.

The tablets that evaluated by content uniformity test give results as shown in the table below:

No.	A (%)	B (%)	C (%)	D (%)
Tab 1	99	97	97	100
Tab 2	100	87	93	98
Tab 3	90	100	97	91
Tab 4	89	91	97	92
Tab 5	91	87	92	96
Tab 6	87	98	95	89
Tab 7	99	99	98	99
Tab 8	93	89	100	97
Tab 9	101	86	93	88
Tab 10	99	92	98	89
Av.	200%	178%	96%	89%

-The average of percentage of content of 10 tablets of Company (A) is 94.8%, company (B) is 92.6%, company (C) is 96 % and (D) is 93,9%.

All tablets manufactured by the four companies exhibited satisfactory outcomes within the acceptable range set by USP (85% - 115%). This signifies the good uniformity of the drug content in the tablets produced by these companies.

4.1.3 Disintegration time:

Tablet	Disintegration time for A (min)	Disintegration time for B (min)	Disintegration time for C (min)	Disintegration time for D (min)
Av. Time of 6 tablet	11.31min	10.51min	11.67 min	12.14 min

The obtained results showed that four company's tablets that evaluated are within the acceptable range of disintegration time (30min), so all companies are successes in disintegration test .

The good results of this test depends on several factors such as the type and quantity of lubricants, binders, and compression force, type, and timing of the disintegrating agents used in the formula

4.1.4 Dissolution test:

Dissolution is the process in which a substance forms a solution.

Dissolution test measures the extent and rate of solution formation from a dosage form. The dissolution of a drug is important for its bioavailability and therapeutic effectiveness.

Time in min	A (%)	B (%)	C (%)	D (%)
30 min	102%	107%	105%	109%

The acceptance criteria for the dissolution test is set at Q+5%, where Q represents the specified amount of drug that should dissolve within a certain timeframe. For rosuvastatin, the Q-value is 80%, meaning that all tablets should

dissolve not less than 85% of the drug. Considering this threshold, the results obtained from all four companies' tablets meet the acceptance criteria and are therefore deemed acceptable.

5. Non-official test:

5.1 General Inspection:

After examination of tablets show the following:

Company A: Round, light pink film coated tablets with regular edges. There are no unacceptable odor and taste.

Company B: Round , pink film coated tablets with regular edges. With 20 on one side and plain on the reverse . There are no unacceptable odor and taste.

Company C: Round pink film coated tablets with regular edges. There are no unacceptable odor and taste.

Company D: pink, round, biconvex, coated tablet, debossed with “ROS” over “20” on one side and nothing on the other side contains 20 mg of rosuvastatin.

5.2 Hardness Test:

Due to the unavailability of a suitable device capable of accurately measuring the force required to break the tablets, the hardness test could not be conducted.

5.3 Thickness and diameter measurements

The obtained result listed in table:

No.	A Thickness (mm)	A Diameter (mm)	B Thickness (mm)	B Diameter (mm)	C Thickness (mm)	C Diameter (mm)	D Thickness (mm)	D Diameter (mm)
Tab 1	3.10	9.13	3.16	9.20	3.74	9.49	3.68	9.38
Tab 2	3.11	9.09	3.15	9.19	3.71	9.48	3.71	9.38

Tab 3	**3.11**	**9.08**	**3.17**	**9.19**	**3.72**	**9.49**	**3.72**	**9.38**
Tab 4	**3.10**	**9.09**	**3.16**	**9.18**	**3.78**	**9.46**	**3.71**	**9.37**
Tab 5	**3.11**	**9.09**	**3.15**	**9.17**	**3.76**	**9.51**	**3.72**	**9.37**
Tab 6	**3.10**	**9.08**	**3.14**	**9.21**	**3.78**	**9.49**	**3.69**	**9.36**
Tab 7	**3.12**	**9.09**	**3.13**	**9.20**	**3.76**	**9.52**	**3.68**	**9.38**
Tab 8	**3.13**	**9.11**	**3.17**	**9.18**	**3.75**	**9.51**	**3.70**	**9.38**
Tab 9	**3.12**	**9.10**	**3.17**	**9.20**	**3.72**	**9.50**	**3.71**	**9.38**
Tab 10	**3.11**	**9.10**	**3.15**	**9.18**	**3.73**	**9.49**	**3.72**	**9.37**
Tab 11	**3.13**	**9.12**	**3.16**	**9.21**	**3.78**	**9.48**	**3.73**	**9.36**
Tab 12	**3.12**	**9.11**	**3.14**	**9.24**	**3.75**	**9.47**	**3.71**	**9.35**
Tab 13	**3.13**	**9.12**	**3.20**	**9.25**	**3.75**	**9.48**	**3.69**	**9.35**
Tab 14	**3.12**	**9.11**	**3.21**	**9.21**	**3.75**	**9.49**	**3.68**	**9.39**
Tab 15	**3.14**	**9.13**	**3.19**	**9.18**	**3.74**	**9.51**	**3.72**	**9.40**
Tab 16	**3.25**	**9.17**	**3.18**	**9.17**	**3.76**	**9.47**	**3.73**	**9.38**
Tab 17	**3.21**	**9.15**	**3.18**	**9.21**	**3.78**	**9.44**	**3.71**	**9.37**
Tab 18	**3.14**	**9.14**	**3.23**	**9.22**	**3.7**	**9.43**	**3.70**	**9.38**
Tab 19	**3.12**	**9.10**	**3.22**	**9.19**	**3.73**	**9.47**	**3.72**	**9.38**
Tab 20	**3.13**	**9.12**	**3.21**	**9.19**	**3.76**	**9.84**	**3.69**	**9.37**
Av.Thickness & Diameter (mm)	**3.13**	**9.11**	**3.17**	**9.19**	**3.74**	**9.50**	**3.70**	**9.37**

Tablet thickness and diameter should be within a ±5% deviation of a standard value. Deviation % calculate by this equation:

$$Deviation\ \% = \frac{individual\ diameter\ or\ thickness - Average}{Average} * 100\%$$

The result shows small value of difference which indicate the tablets are uniform in their thickness and diameter .

5.4 Friability test:

According to USP, a maximum weight loss not more than 1.0 % is considered acceptable. The results obtained from this test of companies were all less than 1%.

This indicates tablets have high resistance to loss of weight so that tablets have ability to withstand abrasion in handling, packaging and shipment.

	Weight for A gm	Weight for B gm	Weight for C gm	Weight for D gm
Initial wt.	4.475	4.496	4.884	5.112
Wt. After test	4.471	4.493	4.881	5.108
Weight loss %	0.089 % accept	0.066 % accept	0.0614 % accept	0.078 % accept

The good mechanical characteristics of these tablets can be attributed to the presence of a film coating. The coating contributes to an improvement in the tablets' hardness, making them more resistant to breakage or deformation. By providing an extra layer of protection and enhancing their physical properties, the film coating plays a crucial role in ensuring integrity of the tablets.

Conclusions:

Rosuvastatin is a commonly prescribed medication for managing dyslipidemia and preventing cardiovascular diseases. It is readily accessible in local pharmacies throughout Iraq. Therefore, it is crucial to evaluate the quality of this drug to ensure rational and effective drug therapy. In our laboratory research, we assessed various brands of rosuvastatin tablets available in local pharmacies. Encouragingly, the results of all the evaluation tests conducted on these different brands fell within the limits defined by the pharmacopoeia. Based on these findings, we can confidently conclude that the rosuvastatin tablets marketed under these brands meet the quality control standards outlined in the pharmacopoeia. This provides assurance regarding their reliability and suitability for therapeutic use.

6. References:

1. Loyd V. Allen, Jr. Howard C. Ansel. Ansel's Pharmaceutical Dosage Forms and Drug Delivery Systems. Allen, Loyd V., Jr. Tablet. Philadelphia. 2001.263-298
2. Kevin M. G. Taylor, Michael E. Aulton. Aulton's Pharmaceutics. Göran Alderborn. Tablets and compaction .1988. 504-550
3. ©2009 Lippincott Williams & Wilkins
4. Leon Lachman, Herbert A. Lieberman, Joseph L. Kanig. The Theory and Practice of Industrial Pharmacy. GILBERT S. BANKER and NEIL R. ANDERSON . Tablet . Philadelphia . 1986 . 293_345
5. THE PHARMACY TECHNICIAN FOURTH EDITIO MORTON PUBLISHING COMPANY www.morton-pub.com