University of Basrah

College of Pharmacy

In vitro Evaluation of Ibuprofen Tablet Dosage Form Of Different Commercially Available Brands In Basrah

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

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ABSTRACT

Ibuprofen is a non-steroidal anti-inflammatory drug (NSAID) that possesses anti-inflammatory, analgesic, and antipyretic effects and it is widely marketed in the Republic of Iraq.

The study aims to evaluate the in vitro quality of four ibuprofen (film and sugar) coated tablets 400mg formulations that are commercially most commonly used in the Republic of Iraq markets.

Ibuprofen tablets were tested include non-pharmacopoeia (non-official) tests like organoleptic properties, friability, thickness, diameter and hardness, and some pharmacopoeia (official) tests according to USP like the uniformity of weight, disintegration time, dissolution, and analysis of the drug active content with the UV spectrophotometric method following comparisons with official protocols and pharmacopeia monograph.

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

1. Introduction

According to united states pharmacopeia (USP), tablets are solid, flat or biconvex unit dosage form of a medicament alone or medicament along with excipients prepared by compressing technique. They may vary in size, shape and weight depending on the medicament and its mode of administration.

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. Most of the medicaments can be processed into tablets but there are some exceptions like medicaments with low density characters, hygroscopic and the medicaments which were not possible to administer. Post-compression studies (Evaluation parameters) plays a major role to release any dosage form into the market. [1]

1.1 Classification of tablets dosage form [2]

Tablets are classified according to their routes of administration or functions. The following are the four main classification groups**:-**

A. Tablets ingested orally:

Ex: Compressed tablets and coated tablets

B. Tablets used in the oral cavity:

Ex: Sublingual tablets, buccal tablets.

C. Tablets administered by other routes:

Ex. Implantation tablets and vaginal tablets

D. Tablets used to prepare solutions:

Ex: Effervescent tablets and dispensing tablets.

1.2 Advantages [3]

As advantages of tablet over other oral dosage form, we have:

- Unit dosage forms with dose precision.
- Least content variability.

- Administration of accurate amounts of minute doses of a drug is possible.
- Economical of all oral dosage forms as its production doesn't requires additional processing steps.
- Easy transportation.
- Sustain release of a drug can be achieved through enteric coating.
- Medicaments with bitter taste can be masked with coating technique (Sugar coating).
- Tablet dosage form is stable when compared to all oral dosage forms.

1.3 Disadvantages [4]

- Administration of drugs is not easy in case of children.
- Drugs with slow dissolution is not acceptable for tableting with good bioavailability.
- Medicaments with low density characters and amorphous in nature are difficult to compress.
- Hygroscopic nature of drugs is not acceptable for tablet compression.

1.4 Evaluation

In pharmacy, the aim of evaluation of tablets is to ensure safety, potency, efficacy, stability, Patient acceptability and patient compliance of tablet, check whether a pharmaceutical tablet satisfy certain standards to claim it to be a quality drug or not, check that the quality parameters are within the acceptance limits or not.

Generally, the evaluation of tablets is done using a number of tests which can be classified into:

1.4.1 The official tests [8]

- ✓ **Weight variation test**

Tablets generally are manufactured to contain a certain amount of active ingredients in a certain weight of tablet. Allowed limits according to U.S.P are shown in figure (1).

Average Weight of Tablet (mg)	Maximum (%) Weight Difference Allowed
130 or less	±10 %
130—324	±7.5%
More than 324	±5%

Figure (1): USP Allowance limits for weight variation test

✓ **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 depending on the following criteria:

❑ The acceptable potency range for (low-dose, highly potent drugs) = 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**

The first thing that happens to tablets before absorption is disintegration, or breaking down to granules and small particles before dissolving (dissolution) in the gastric fluid.

For absorption to take place, dissolution of the drug in the gastrointestinal fluid has to occur, since only the drug in solution is absorbed.

The time it takes to disintegrate is called disintegration time which can be experimentally measured by a USP disintegration apparatus.

✓ **Dissolution**

Dissolution is the process by which a solid solute enters a solution. Pharmaceutically, it may be defined as the amount of drug substance that goes into

solution per unit time under standardized conditions of liquid/solid interface, temperature and solvent composition. Dissolution kinetics is important in determining the bioavailability of a drug.

1.4.2 Non-official tests [9]

- ✓ **General Inspection**

Includes a visual inspection and identification for any flaws that may affect the appearance for several reasons such as:

❑ To control and check batch to batch uniformity.

❑ To control any manufacturing issues.

❑ To ensure consumer acceptance.

This inspection includes organoleptic properties of tablet like colour, odour, any physical flaws…. etc.

Many pharmaceutical tablets use the colour as vital means of rapid identification and consumer acceptance. The color of a product must be uniform within a single tablet.

- ✓ **Size and shape**

Measured by:

- ❖ Micrometer
- ❖ Sliding calliper scale

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

More likely to cause capping problem.

- ✓ **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 and can be measured using hardness tester.

✓ **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, can be measured using the friability tester.

1.5 Drug under investigation (Ibuprofen)

Ibuprofen is a nonsteroidal anti-inflammatory drug. It is non-selective COX inhibitor, which means it inhibits both COX-1 and COX-2 enzymes. COX-2 inhibition leads to decreases in production of prostaglandins which is responsible for the transmission of pain signals in the body and mediating inflammation, fever and swelling.

It is used to reduce fever and treat pain or inflammation caused by many conditions such as headache, toothache, back pain, arthritis, menstrual cramps, or minor injury. [3]

Table (1) illustrate the physicochemical properties of Ibuprofen.

Table (1)

Physiochemical Properties

S. NO.	PHYSICAL AND CHEMICAL PROPERTIES	
1	Molecular weight	206.28 g/mol
2	Physical appearance	Colorless crystalline solid
3	Melting point	75–77°C
4	Solubility	Very soluble in alcohol
5	Octanol/water partition coefficient	3.97
6	Presence of ring	Phenyl
7	Number of chiral centers	1

Ibuprofen is a carboxylic acid (Propionic acid derivative), as seen in its chemical structure, figure (2), has a relatively high lipophilicity and shows poor solubility in an aqueous media this due to the presence of the non-polar alkyl groups and benzene ring which significantly reduces the polarity of the ibuprofen molecule. Ibuprofen is soluble in organic solvents such as ethanol, DMSO, and dimethyl formamide. The solubility of (±)-ibuprofen in these solvents is approximately 60, 50, and 45 mg/ml, respectively.

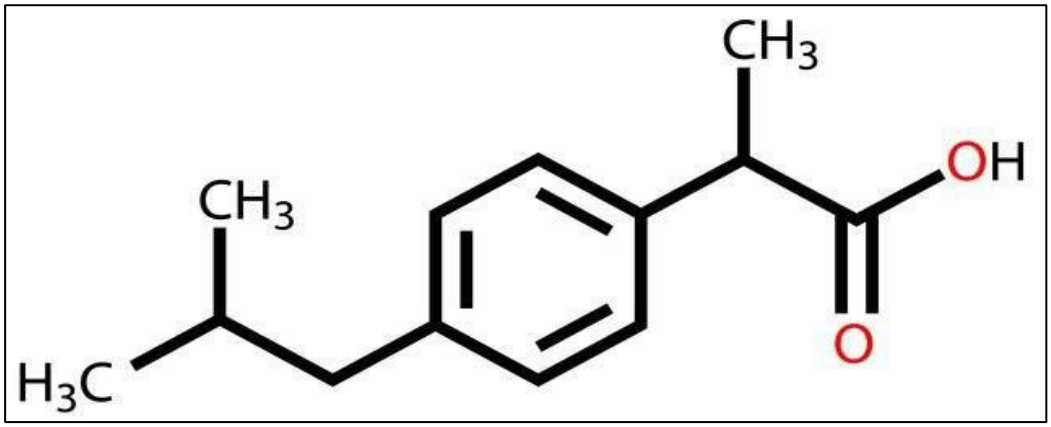

Figure (2): The chemical structure of Ibuprofen

The main objective of study was to evaluate the commercially available Ibuprofen tablets using different tests include non-pharmacopoeial (non-official) tests like organoleptic properties, friability, thickness, diameter and hardness, and some pharmacopoeial (official) tests according to USP like weight variation , content uniformity , *In vitro* disintegration and dissolution tests.

2. Experimental work

2.1 Materials

Film and sugar Ibuprofen coated tablets (strength of 400 mg) of four different companies coded as (A, B, C, and D), absolute ethanol, distilled water, monosodium phosphate and disodium phosphate.

2.2 Equipment (see appendix I)

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

2.3 Methods

2.3.1 Weight Variation Test

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

Individual weights are compared with the average weight. If no more than two tablets are outside the percentage limit, and if no tablet differs by more than two times the percentage limit, the tablets pass the USP weight variation tests.[5]

2.3.2 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 at 263.5 nm. Use the calibration curve to calculate the recovered concentration of ibuprofen 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). [6]

2.3.3 Disintegration Test

To carry out a disintegration test for tablets, we use the U.S.P. device (disintegrator) in which six glass tubes that are 3 inches in length; open at the top and 10 mesh screen at the bottom end. To estimate disintegration time, six tablets were randomly taken from 18 tablets of each company, one tablet is placed in each tube and the basket rack is positioned in a 1-L beaker of water, simulated gastric fluid or simulated intestinal fluid at 37 ± 2°, then raised and lowered into a beaker of water. If the tablets float, perforated plastic disks are placed on the top of the tablets to keep them under the water level. The tablet disintegration time is taken when no residue is left in the mesh. Unless otherwise stated in the individual monograph film-coated tablets disintegrate within 30 minutes and other coated tablets disintegrate within 60 minutes.

2.3.4 Dissolution Test

This test determines the amount of active ingredient(s) released from a solid oral dosage form, under controlled conditions (Temp. about 37C, stirring speed= 50rpm at 900ml of phosphate buffer (pH =7.4) within a predetermined length of time).

One tablet of each companies was taken (this due to short time and lack of required materials in sufficient quantities), then was put in single jar of dissolution tester. Dissolution apparatus start for 30min, after that withdraw sample from each jar and filtered it. Then assay by UV spectrophotometer employing UV absorption at the estimated wave length of maximum absorbance. Then the prepared calibration curve was used to obtain the concentration for each. [2]

Tolerance of test was not less than 80% of the labelled amount of ibuprofen is dissolved in 30 min.

2.3.5 General Inspection

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

2.3.6 Thickness and Diameter Tests

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

2.3.7 Hardness Test

Six tablets were placed individually between two anvils, force is applied to the anvils by using hardness tester & the crushing strength that just causes the tablet to break is recorded (in kg). Tablet hardness should be between 6 – 10 kg in range.

2.3.8 Friability test

Twenty tablets were randomly selected and weighed by the sensitive digital balance to read pre-test weight. Then we put the tablet in friabilator to rotate them for 4

minutes (100 rotate). After that, we take the tablets out of the machine and try to clean them with a brush from crumbs and dust, then we weigh the tablets again by balance to obtain post-test weight. The weight loss% was calculated by the following equation:

Weight loss% = (W1 - W2/W1) *100% ---------- (1)

w1= Initial weight of tablets or pre-test weight.

w2= Final weight of tablets or post-test weight.

Friability Limits: According to USP, IP and BP, it should be not more than 1.0%.

3. Results and discussion

In our study, Ibuprofen tablets 400mg of four different companies (A, B, C, and D) have been evaluated through official and non-official tests. These tests were performed by use standard equipment and methods.

3.1 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 percentage =5%.

The weight of each of twenty ibuprofen tablets of each company was measured as well as the standard of deviation. The results are listed in Table (2).

Table (2)

No.	A (Tablet wt. in g)	B (Tablet wt. in g)	C (Tablet wt. in g)	D (Tablet wt. in g)
Tab 1	**0.591**	**0.638**	**0.638**	**0.877**
Tab 2	**0.592**	**0.650**	**0.633**	**0.863**
Tab 3	**0.581**	**0.644**	**0.637**	**0.848**
Tab 4	**0.575**	**0.631**	**0.635**	**0.875**
Tab 5	**0.574**	**0.641**	**0.642**	**0.891**
Tab 6	**0.567**	**0.636**	**0.634**	**0.900**
Tab 7	**0.579**	**0.647**	**0.633**	**0.877**
Tab 8	**0.580**	**0.635**	**0.628**	**0.833**
Tab 9	**0.579**	**0.639**	**0.639**	**0.840**
Tab 10	**0.576**	**0.640**	**0.644**	**0.894**
Tab 11	**0.580**	**0.650**	**0.643**	**0.848**
Tab 12	**0.577**	**0.642**	**0.636**	**0.844**
Tab 13	**0.577**	**0.645**	**0.626**	**0.891**
Tab 14	**0.579**	**0.637**	**0.637**	**0.900**
Tab 15	**0.572**	**0.645**	**0.635**	**0.897**
Tab 16	**0.588**	**0.638**	**0.637**	**0.885**
Tab 17	**0.576**	**0.651**	**0.642**	**0.909**
Tab 18	**0.586**	**0.643**	**0.641**	**0.827**
Tab 19	**0.581**	**0.646**	**0.637**	**0.838**
Tab 20	**0.586**	**0.646**	**0.632**	**0.868**
Av.wt	**0.580**	**0.642**	**0.636**	**0.870**
Accepted Range (+ 5%)	**0.551-0.609**	**0.610-0.674**	**0.604-0.668**	**0.827-0.914**

The results indicate that all tablets of each company were within USP weight limits. The lowest weight variation was found among tablets of company (C). The reasons of low weight variation between tablets attributed to good flowability, uniform size and shape of powder particles and the appropriate amount and type of excipients. The company (D) showed variation in weight more than other companies but is still within accepted range of USP.

3.2 Content uniformity test

This test was performed to ensure that every tablet contains the same amount of drug substance with a defined allowed variation within a batch. Calibration curve of Ibuprofen in ethanol, figure (3)-a, was used to estimate the required concentration of ibuprofen that present in each tablet.

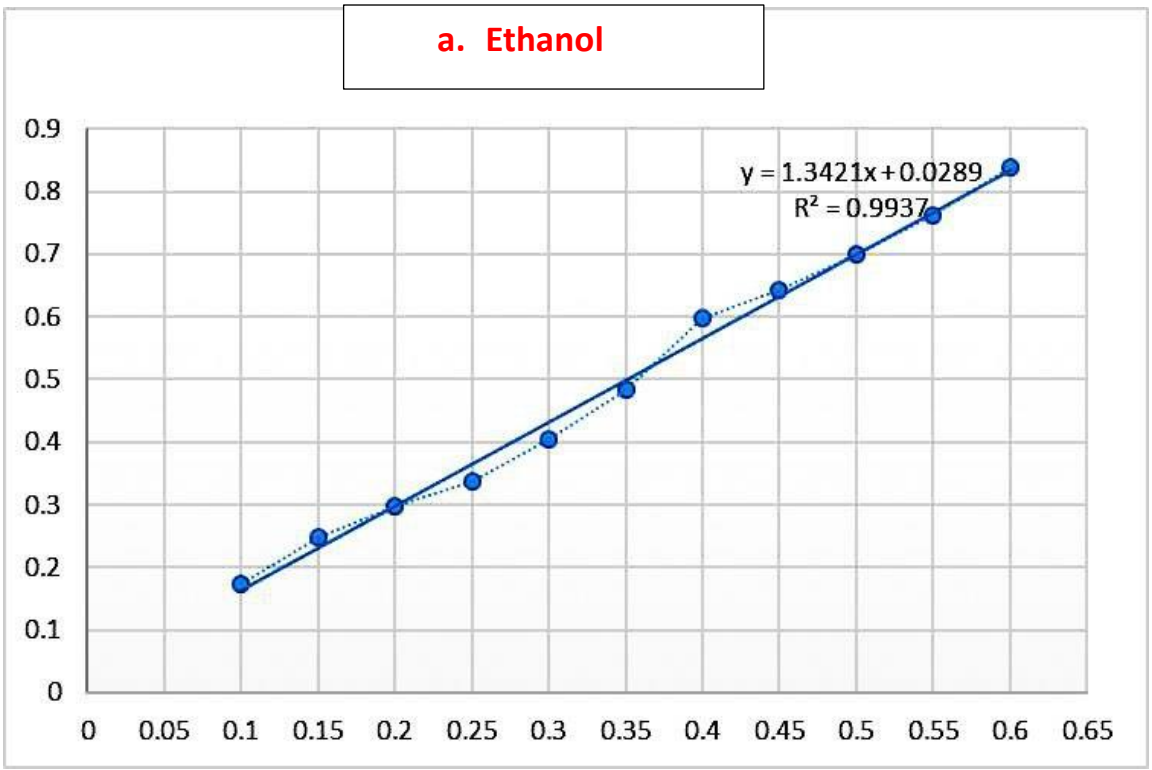

Figure (3): Calibration curves of Ibuprofen in (a) ethanol and (b) phosphate buffer

The results of content uniformity test were illustrated in Table (3).

Table (3)

No.	A (%)	B (%)	C (%)	D (%)
Tab 1	**100**	**96**	**97**	**98**
Tab 2	**98**	**107**	**91**	**100**
Tab 3	**92**	**107**	**91**	**86**
Tab 4	**86**	**88**	**96**	**86**
Tab 5	**87**	**88**	**91**	**95**
Tab 6	**85**	**96**	**96**	**90**
Tab 7	**97**	**103**	**96**	**96**
Tab 8	**94**	**86**	**96**	**88**
Tab 9	**100**	**86**	**95**	**85**
Tab 10	**102**	**99**	**92**	**89**
Av.	**94.1%**	**95.6%**	**94.1%**	**91.3%**

The average of percentage of content of 10 tablets of Company (A) is 94.1%, company (B) is 95.6%, company (C) is 94.1% and (D) is 91.3%. Depending on the acceptable range stipulated by USP (85% - 115%), all tablets of the four companies showed acceptable results. This indicate good uniformity of drug in the prepared tablets.

Although tablets of company B with highest average percentage of content but they show variation in drug content among ten tablets in range (86 -107%). While tablet of company C showed better results, where all tablets within range (91-97%).

The range (85-115%) reflect the acceptable percentage of content that limit effectiveness of drug, less than 115% is effective drug and nontoxic and less than 85% is nontoxic but not provide therapeutic effect.

3.3 Disintegration time

The obtained results showed that the four brands tablets were disintegrated within the accepted disintegration time (30min). The results reflected fast disintegration time values as seen in Table (4). The faster disintegration time will improve the dissolution rate and this enhance absorption and bioavailability and provide rapid onset of action and response.

Table (4)

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	1.53min	1.45min	2.03min	2.3min

The good results of this test may be due to several factors such as: amount and type of disintegrant that used in formula, in addition to type and amount of lubricant, binder and compression force.

3.4 Dissolution Test

Dissolution is the process in which a substance forms a solution. Dissolution testing 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. To evaluate the dissolution of drug products properly, it is critical for procedures to be standardized. This standardization helps to show consistent quality in production and may serve as a predictive measure of efficacy. The calibration curve, figure (4), will be used to obtain the amount that released from tablet after 30min:

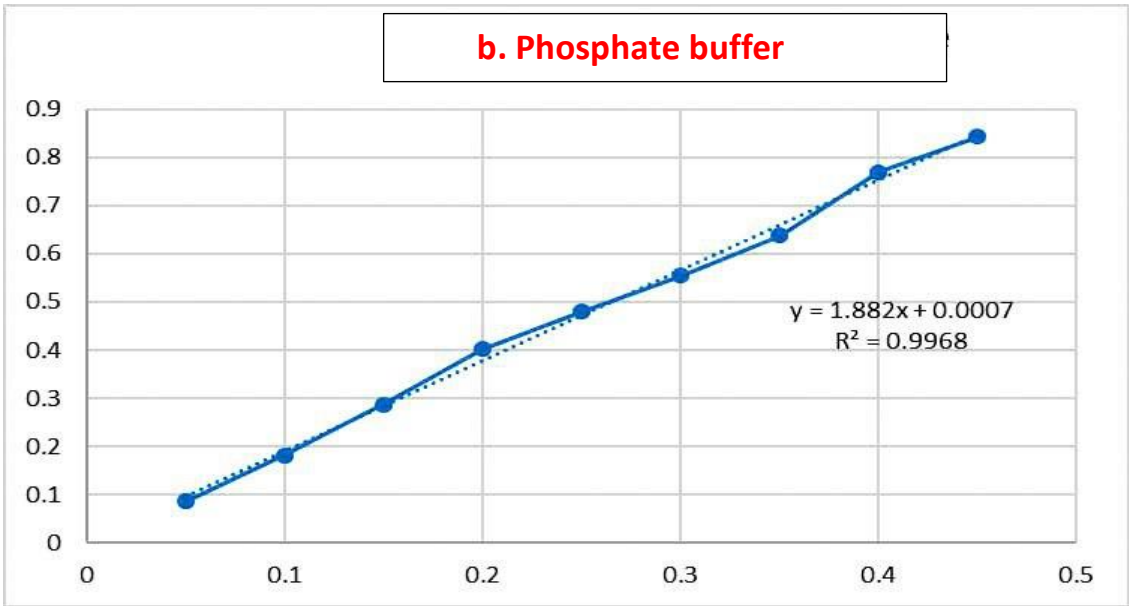

Figure (4): Calibration curve of Ibuprofen in phosphate buffer (pH = 7.4)

Acceptance criteria of dissolution test is =Q+5%, Q= the amount of drug that should dissolved in certain time. Each drug has different Q according USP. Q-value of ibuprofen is 80% so the acceptable criteria must all tablets not less than 85%. Based on this limit so all obtained results of four companies are accepted as seen in Table (4). The amount that is obtained from dissolution test after 30min is high and exceed 100٪ this may be attributed to tablets that show more than 100% in content uniformity. Company (B) show high result in dissolution and content but it is still within acceptable limit. Higher dissolution results reflected higher bioavailability.

Table (5)

Time in min	A (%)	B (%)	C (%)	D (%)
30 min	101%	109%	102%	105%

3.5 General Inspection

Appearance is the first most required quality for the acceptance of tablet. General elegance and its identity play a major role for the consumer acceptance. Acceptance of the appearance of batches of the tablet has been done based on the measurement of the following factors like colour, shape, presence or absence of odour and taste.[4]

After examination of tablets, the following observation were obtained:

Company A: Round, dark pink film coated tablets with regular edges. The tablets without a break-line and any engraving. There are no unacceptable odour and taste.

Company B: Oval pink film coated tablets with regular edges. Without a break -line and any engraving. With acceptable odour and slightly bitter taste.

Company C: Round pink film coated tablets with regular edges. On its surface there is an engraving (400). With acceptable odour and taste.

Company D: Round, white sugar-coated tablets with regular edges. With Sweet taste and acceptable odour. Without break line and any engraving.

The tablets of each company have a good appearance, this may be attributed to the coating, which provides taste masking, odour and gives a smooth finish to the product and makes it easy to swallow. The coating enhances product acceptance and the appearance of the tablet. [7]

Appearance properties are very important to identification and acceptance by patients. In addition to that are markers for tablets stability for example the presence of odour in a batch of tablet indicates a stability problem.

3.6 Thickness and diameter measurements

The experiment is conducted to test the uniformity of the tablets thickness and diameter. The obtained result listed in Table (6):

Table (6)

No.	A Thickness (mm)	A Diameter (mm)	B Thickness (mm)	C Thickness (mm)	C Diameter (mm)	D Thickness (mm)	D Diameter (mm)
Tab 1	7.67	12.86	6.60	5.59	13	7.67	13.56
Tab 2	7.84	12.85	6.63	5.61	12.99	7.84	13.53
Tab 3	7.88	12.88	6.56	5.57	13	7.88	13.57
Tab 4	7.78	12.86	6.59	5.59	13.08	7.78	13.53
Tab 5	7.85	12.87	6.49	5.61	12.99	7.85	13.58
Tab 6	7.82	12.88	6.57	5.57	13.06	7.82	13.56
Tab 7	7.82	12.87	6.59	5.55	13.01	7.82	13.56
Tab 8	7.99	12.86	6.58	5.6	12.97	7.99	13.5
Tab 9	7.75	12.88	6.58	5.58	12.99	7.75	13.58
Tab 10	7.75	12.88	6.58	5.58	12.93	7.75	13.56
Tab 11	7.76	12.84	6.56	5.6	13.04	7.8	13.53
Tab 12	7.98	12.86	6.6	5.6	13.04	7.98	13.52
Tab 13	7.91	12.86	6.58	5.58	13.01	7.91	13.55
Tab 14	7.8	12.86	6.6	5.61	12.96	7.8	13.53
Tab 15	7.78	12.86	6.58	5.62	12.93	7.78	13.57
Tab 16	8.02	12.87	6.62	5.58	13.02	8.02	13.53
Tab 17	7.86	12.85	6.61	5.61	13	7.86	13.51
Tab 18	7.7	12.87	6.56	5.6	13	7.7	13.53
Tab 19	7.72	12.83	6.62	5.62	13.06	7.72	13.56
Tab 20	7.65	12.86	6.62	5.62	12.98	7.65	13.57
Av.Thickness & Diameter (mm)	7.8165	12.8625	6.586	5.5945	13.003	7.8185	13.5465

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. Thickness and diameter must be controlled. The uniformity in diameter and thickness of tablets is very important to increase the patient compliance and avoid them from being confused with different sizes of the tablets. Different sizes of the tablets may cause the patient to think that the drugs or tablets have different amount of active ingredient.

Thickness of a tablet is determined by the diameter of the die, the amount of fill permitted to enter the die, the compaction characteristics of the fill material, and the force or pressure applied during compression. Many of these factors are affected by the flow properties of powders, size and shape of particles and the amount and type of excipients (glidants). To produce tablets of uniform thickness during and between batch productions for the same formulation, care must be exercised to employ the same factors of fill, die, and pressure.

3.7 Friability test

Is used to test the durability of tablets during packaging processes and transit. This test performed to determine the mechanical strength of tablets through measuring the weight loss %. According to USP, a maximum weight loss not more than 1.0 % is considered acceptable. The results obtained from this test of companies as shown in Table (7), were all less than 1%. This indicates that tablets have high resistance to loss of weight so that tablets have ability to withstand abrasion in handling, packaging and shipment.

Table (7)

	Weight for A (gm)	Weight for B (gm)	Weight for C (gm)	Weight for D (gm)
Initial wt.	**11.6394**	**12.9852**	**12.8699**	**17.4148**
Wt. After test	**11.6370**	**12.9825**	**12.8693**	**17.4140**
Weight loss %	**0.0206 % Accepted**	**0.0208 % Accepted**	**0.00466 % Accepted**	**0.00459 % Accepted**

The good mechanical properties of these tablets it is attributed to sugar and film coated. Coating provides stability to the tablets in handling and prevents them from sticking together. The coating also improves the hardness of the tablets.

We note that the lowest weight lost was from the company (D) this is due to that company D tablets are sugar coated. Sugar coating is a multistage process in which a thick and hard sugar coat is spread over the surface of tablets. While film coating is single stage process including spread a thin layer over the surface of tablets.

4. Conclusions

From the laboratory work that we conducted for a number of companies available in local pharmacies, it was found that the results of all these evaluation tests of different companies of Ibuprofen tablets were within the pharmacopoeia limits so it could be concluded that marketed pharmaceutical tablets of Ibuprofen of these brands satisfy quality control limits of pharmacopoeia.

5. Acknowledgement

Praise be to the Lord of the world (Allah), and prayer and peace upon the most honoured prophets and messengers Mohammed and on his family and his companions to the doomsday.

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Appendix I