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A comparative study of amlodipine marketed products and their quantitative evaluation by UV – spectrophotometrys

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Abstract

The present work deals with the comparative study of six different brands of Amlodipine and their Quantitative Evaluation by UV Spectrophotometry. The Evaluation of pharmaceutical equivalency of all the six marketed brands of Amlodipine (5 mg) was done by Quantitative evaluation, Weight variation test, Disintegration test, Friability test and Cost analysis. Objective of the present work is to report the best drug among the six brands also to give a suitable and better method for the comparative study. The Method employs Double Beam UV spectrophotometer [LAB INDIA-UV 3000^{+} (version 3.5)]. The selected solvent used was Methanol and the detection was carried out at a wavelength 237 nm. The Calibration graph of Amlodipine and the six brands of Amlodipine were found to be linear with a Regression Coefficient of 0.98 which falls within the limits of Beer-Lamberts law. It was found that Weight Variation Test of Amlodac-5 and Stamlo-5 were not in the acceptance limits and the remaining four tablets passes the Weight Variation test i.e., they lie within the acceptance limits of (±7.5). The percentage of friability for Amlokind-5 was found to be 0.649% which was less than 0.8%(normal limits) and the remaining brands were found out of limits with little variations. The Disintegration time was found to be 10 seconds (Fastest release) for Amlopres-5 and 4.43 minutes (Slowest release) for Amlodac-5. The tablet Amlokind-5 was found to be best among all the six brands as it is within the acceptable limits. And this method of Quantitative Evaluation was simple, rapid and economical. Hence it can be successfully utilized for comparative studies in routine Lab analysis.

Keywords: UV Spectrophotometry, Quantitative evaluation, Amlodipine

INTRODUCTION

The World Health Organization has identified Hypertension or High blood pressure as the leading cause of cardiovascular mortality

Hypertension or high blood pressure

is a chronic medical condition of heart in which systemic arterial pressure is increased. Normal blood is below 120/80 mm of Hg. Blood pressure between 120/80 and 139/89 mm of Hg is called Pre-Hypertension and blood pressure of 140/90 mm of Hg and above is considered High blood pressure.

Types of hypertension: Hypertension is classified into two types

- Primary or essential hypertension
- Secondary hypertension

AIM AND PLAN OF WORK

Aim

The aim of the present work is to do a comparative study of different brands of Amlodipine and their quantitative analysis by UV spectrophotometry. These tests are necessary to ascertain the claim of pharmaceutical equivalency by most generic companies.

Plan of work

The experimental work has been planned as follows:

- Review of literature for Amlodipine regarding its physical and chemical properties and the previous analytical methods that were conducted on this drug forms the basis for quantitative evaluation of different brands of Amlodipine.
- Selection of solvent to be used as diluent.
- Choosing the suitable solvent in which drug is soluble and stable they must be easily available and economical.
- A perfect study of structure of drug and its physico-chemical properties and review of literature to select the spectrophotometric parameters.
- Assessment of pharmaceutical equivalency of different brands of Amlodipine through quantitative evaluation, and also friability test, disintegration test, weight variation test and cost analysis.

MATERIALS AND METHODS

Instruments and chemicals

I. Instruments

S.No	Name	Model
1.	UV-VIS spectrophotometer	LAB INDIA-UV 3000^{+} (version 3.5) Double beam.
2.	UV-software	UV WIN-5 spectrophotometer software (version 5.20)
3.	Digital balance	AFCOSET modern electronic balance (ER-180A)
4.	Sonicator	Ultra-sonic
5.	Friabilator	LAB INDIA tablet friability tester- FT 1020
6.	Disintegration test apparatus.	LAB INDIA DT 1000.

II. Chemicals

S. No.	Name	Specification
1.	METHANOL	Grade-AR
2.	WATER	Double distilled water
3.	0.1N HCL	Grade-AR

III. Active pharmaceutical ingredient

S.NO	Name	Grade/Batch No.
1.	AMLODIPINE BESYLATE USP	Aurobindo laboratories, Batch no. :HALC09100010

IV. Marketed formulations

S.NO	Brand names	Manufacturers	Batch no.
1.	AMLOKIND-5	Mankind Pharma Ltd.	A1AFL121
2.	AMLOPIN	USV Ltd.	48001347
3.	AMCARD	Systopic Lab Pvt.Ltd.	AY250912
4.	STAMLO-5	Dr. Reddy's Lab.Ltd.	E300094
5.	AMLODAC-5	Zydus Health Care	ZHM2660
6.	AMLOPRES-5	Cipla Ltd.	A22031

Quantitative evaluation

Calibration of standard amlodipine

Preparation of standard amlodipine

- Weigh 50mg of standard amlodipine using Afcoset modern electronic balance(ER-180A).
- Dissolve it in methanol by shaking. The volume was made up to 1000ml with methanol.
- Now the concentration is 1000µg/ml.

Preparations of dilutions of standard drug

- Prepare the dilutions from 10µg to 60µg.

- For preparing 10µg dilution, pipette out 0.1ml from the above concentration i.e 1000µg/ml and transfer it in to 10ml volumetric flask and make up the volume up to the mark.
- Similarly, prepare 20µg dilution by pipetting out 0.2ml from the above concentration i.e 1000µg/ml and transfer it in to 10ml volumetric flask and make up the volume up to the mark.
- To prepare 30µg dilution pipette out 0.3ml from the above concentration i.e 1000µg/ml and transfer it in to 10ml volumetric flask and make up the volume up to the mark.
- To prepare 40µg dilution pipette out 0.4ml from the above concentration i.e 1000µg/ml and transfer it in to 10ml volumetric flask and make up the volume up to the mark.
- To prepare 50µg dilution pipette out 0.5ml from the above concentration i.e 1000µg/ml and transfer it in to 10ml volumetric flask and make up the volume up to the mark.
- To prepare 60µg dilution pipette out 0.6ml from the above concentration i.e 1000µg/ml and transfer it in to 10ml volumetric flask and make up the volume up to the mark.
- After preparing all the dilutions from 10µg-60µg, a blank solution is prepared.

Preparation of blank solution

- A blank solution was prepared by adding 1ml methanol and make up the volume to 9ml using distilled water but without addition of drug(amlodipine besylate).

Procedure

- The absorbance of resulting dilutions were measured using UV-spectrophotometer at 237nm wavelength
- Keep two blanks in uv/vis-spectrophotometer (version 3.5) double beam and set it to zero absorbance.
- Now, remove one blank and keep first dilution sample i.e. 10µg in one cuvette and place it in the instrument. Check it's absorbance, it should be within the limits of regression factor (0.95).
- Plot a calibration curve by taking concentration on x-axis and absorbance on y-axis.

Comparative study of different amlodipine marketed products with standard amlodipine

Procedure

- Weigh the tablets of each brand and note their individual weights.
- Also, take their total weights and average weights.
- Triturate 10 tablets of any one brand in a glass motor to very fine powder.
- Then take 10mg of drug from the grinded powder and add 10ml of methanol to it.
- Shake for half-an hour.
- Filter the above mixture in to a conical flask by filtering it through filter paper.
- Take 1ml from conical flask and make up to 5ml with distilled water.
- Prepare the blank solution by adding 1ml methanol and 9ml distilled water. But without addition of drug.
- See the absorbance in UV-spectrophotometer by keeping one blank and one dilution in cuvettes.
- Similarly, repeat the same procedure for other brands and the % drug content was determined from the absorbance using regression factor obtained in the calibration curve.
- The results obtained are compared with the standard calibration curve.

Other methods of evaluation of pharmaceutical equivalency

Cost analysis

Cost analysis is the accumulation, examination and manipulation of cost data for comparison. Cost analysis studies which focus on antihypertensive drug combinations, however, have been scarce.

The objective of the present cost analysis study is to evaluate and compare the costs of six different marketed brands of Amlodipine_ Stamlo, Amlodac, Amlokind, Amlopres, Amcard, Amlopin. The cost of the marketed drug varies depending upon the cost of production and the excipients used.

Weight variation test

This is an official test in the in process quality control of tablets .It give an idea of possible variation within the same batch by weight variation of tablets. Frequently for every half an hour corrections are made during the compression of tablet if necessary. Any variations in weight of the tablet lead to either under dose or over dose. This is particularly true when the drugs are potent or low dose drugs. The

weight variation test is passed if not more than 2 tablets falls outside the range if 20 tablets were taken and not more than 1 tablet falls outside if only 10 tablets were taken for the test. Improper flow of granules from the hopper is one of the reason for weight variation.

Procedure

Take 20 Tablet and weighed individually. Calculate average weight and compare the individual tablet weight to the average. The percent differences in weight variation should be within limits

*The limit should be +or-7.5 .Calculate the average weight by using following formula

Average weight of tablets = sum of weight of 20 tablets/20

Disintegration test

Disintegration test is a measure of the time required under a given set of conditions for a group of tablets to disintegrate into particles which will pass through a 10 mesh screen. Generally, the test is useful as a quality assurance tool for conventional dosage forms.

Procedure

The disintegration test is carried out using the disintegration tester which consists of a basket rack holding 6 plastic tubes, open at the top and bottom, the bottom of the tube is covered by a 10-mesh screen. The basket is immersed in a bath of suitable liquid held at 37 ^{o}C, preferably in a 1L beaker. For compressed uncoated tablets, the testing fluid is usually water at 37 ^{o}C but some monographs direct that simulated gastric fluid be used.Totest for the disintegration time, a single tablet is placed in each tube, and the basket rack is positioned in a 1-L beaker containing water or simulated gastric fluid, or stimulated out of the assembly(ie.,0.1N HCl because stomach pH is 1-3).

Friability Test

Friability is the phenomenon where the surface of the tablet is damage or shown a site of damage due to mechanical shock".

It can also be defined as "Friability is done to measure the loss of the weight of tablet in the container or package due the removal of fine particles from the surface".

Percentage of friability

The percentage friability of the tablets of a badge can be found by the following formula:

Percentage Friability = $W1 – W_2/W_1 \times 100$

Where, W_1 = weight of tablets before testing

W_2 = weight of tablets after testing.

According to B.P = Percentage of friability should be not more than 0.8%.

According to U.S.P = Percentage of friability should be not more than 4%.

RESULTS AND DISCUSSIONS

Quantitative evaluation

Calibration of standard amlodipine

Acceptance criteria

The regression coefficient of the calibration curve should be 0.988.

Table 1: Calibration of Standard Amlodipine (Conc. v/s Abs at λ=237nm)

S.No	Type	Concentration[µg/µl]	Absorbance
1.	Standard	10.0000	0.356
2.	Standard	20.0000	0.630
3.	Standard	30.0000	0.916
4.	Standard	40.0000	1.205
5.	Standard	50.0000	1.297
6.	Standard	60.0000	1.497

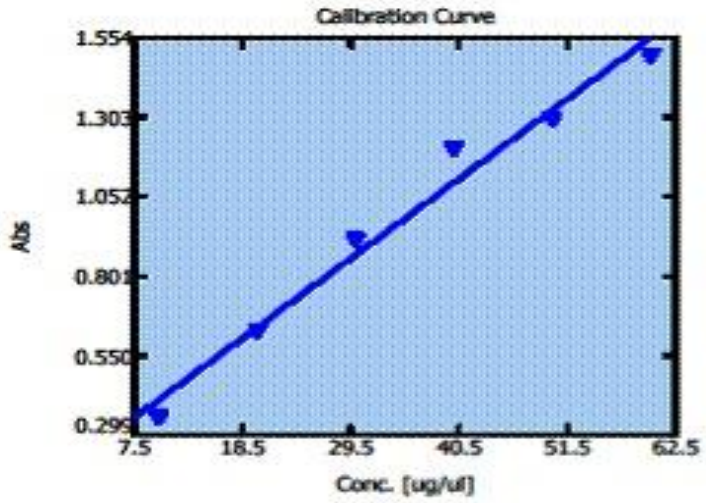

Fig 1: Calibration curve of standard Amlodipine (Conc. v/s Abs at λ=237nm)

Discussion

The Calibration curve obtained was found to be Linear and the value of Regression coefficient was r = 0.98, which falls within the limits of Beer-Lambert's law and hence the results were found to be satisfactory.

Comparative study of different marketed products of amlodipine with standard amlodipine acceptance criteria

The regression coefficient of the calibration curve should be 0.988.

Results

Table -2: Calibration of Different Brands of Amlodipine & Determination of Their Unknown Concentration

Samples	Conc. (µg/µl)	Absorbance
Stamlo-5	22.892	0.7
Amlodac -5	40.533	1.11
Amlokind-5	11.292	0.442
Amlopres-5	5.601	0.312
Amcard -5	17.114	0.575
Amlopin-5	5.951	0.32

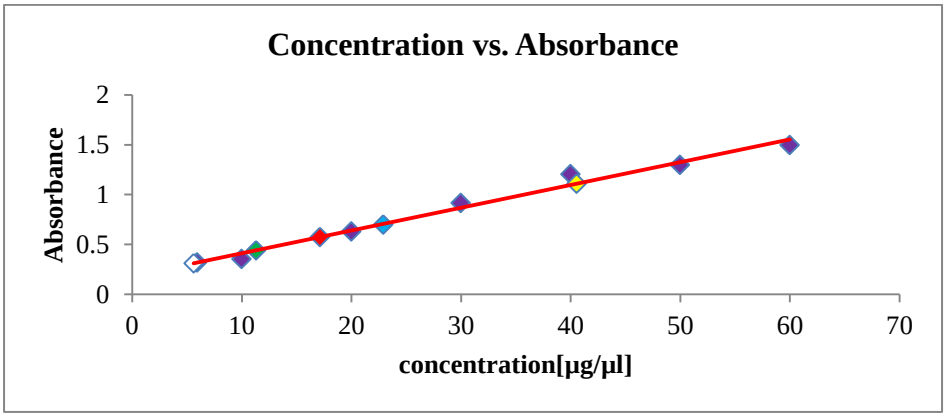

Fig 2: Calibration curve of different brands of amlodipine & determination of their unknown concentration

Discussion

Calibration curve of different brands of Amlodipine was Linear and Regression coefficient was not more than r = 0.98 which falls within the limits of Beer – Lambert's law.

The concentration of Amlodac-5 was found to be high, since it is a sustained release film coated tablet when compared with other brands. Hence the results were found to be satisfactory.

Other methods of evaluation of pharmaceutical equivalency

Cost analysis

Table-3: Cost Analysis

S. No	Brand name	Generics	Manufacturers	Dose	Type	Price
1.	Amlokind-5	Amlodipine	Mankind pharma ltd.	5mg	Tablet	33/-
2.	Amlopin	Amlodipine	Usv ltd.	5mg	Tablet	68/-
3.	Amcard	Amlodipine	Systopic lab pvt. Ltd.	5mg	Tablet	50/-
4.	Stamlo-5	Amlodipine	Dr.reddy's lab ltd.	5mg	Tablet	110/-
5.	Amlodac-5	Amlodipine	Zydus health care	5mg	Tablet	60/-
6.	Amlopres-5	Amlodipine	Cipla ltd.	5mg	Tablet	88/-

Discussion

Stamlo, among all, was found to be available at a higher price than the other five. It is manufactured by Dr. Reddy's labs. The cost variation is found to be due to various excipients like magnesium, calcium & sodium stearates, wetting agents that are anionic surfactants are preferred like sodium lauryl sulphate, suitable anti adherents or glidants are also used like purified talc.Cost might differ for coated and uncoated tablets also; as seen in Amlodac. The excipients used for the film tablet coating are propylene glycols, titanium dioxide etc.

Weight variation test

Acceptance criteria

The percentage difference in weight variation should be within limits, the limit should be ±7.5. The weight variation test is passed if not more than 2 tablets falls out of these range.

Results

Calculations of average weights

Table-4: Individual weights & Average weights of all the brands

S.NO	Brand A Stamlo (grams)	Brand B Amlodac (grams)	Brand C Amlokind (grams)	Brand D Amlopres (grams)	Brand E Amcard (grams)	Brand F Amlopin (grams)
1.	0.07	0.07	0.15	0.116	0.09	0.203
2.	0.08	0.07	0.15	0.123	0.093	0.196
3.	0.07	0.06	0.15	0.117	0.09	0.194
4.	0.06	0.06	0.15	0.12	0.092	0.198
5.	0.07	0.06	0.15	0.122	0.09	0.202
6.	0.07	0.06	0.15	0.124	0.09	0.194
7.	0.06	0.06	0.16	0.12	0.089	0.197
8.	0.06	0.06	0.15	0.126	0.089	0.196
9.	0.07	0.06	0.16	0.121	0.089	0.195
10.	0.07	0.06	0.15	0.121	0.089	0.198
ΣX	0.68	0.62	1.52	1.21	0.901	1.973
X	0.068	0.062	0.152	0.121	0.0901	0.1973

***** ΣX=total sum *****X= arithmetic mean

Discussion

It was found from the above data that Amlodac-5 and Stamlo-5 are not in the given limits. And the remaining 4 tablets pass the weight variation test i.e., they lie within the acceptance limits.

Disintegrationtest

Acceptance criteria

The limits are 15 mins for uncoated tablet, 1 hr for coated tablet and 3 mins for dispersable tablet. This test is not applicable for sustained chewable and sublingual tablets.

- Disintegration time of film coated tablets is 45 mins.
- Highly soluble drugs : solubility at 37± 0.5°C,
- Dose - solubility volume < 250ml at P^H: 1.2- 6.8
- Rapidly dissolving drugs :
- Dissolution > 80% in 15 mins at P^H 1.2, 4.0, 6.8

Results

Table-5: Disintegration Test

S. no	Brandsof amlodipine	Disintegration time
1.	Amlokind-5	Less than 20 seconds
2.	Amcard	Less than 20 seconds
3.	Amlodac-5	4.43 minutes
4.	Stamlo-5	15 seconds
5.	Amlopres-5	10 seconds
6.	Amlopin	45 seconds

Discussion

From the above experimental data we found that Amlopress-5 was having fastest disintegration time of 10 seconds and next was found to be Stamlo-5 with disintegration time of 15 secondsand we observed that Amlodac -5 was having the slowest disintegration time because it was a film coated tablet.

Friability test

Acceptance criteria

Permitted percentage friability should not be more than 0.8%.

Results

Table-6: Friability Test

S.no	Brand name	Initial weight(grams)	Final weight(grams)	% friability	% loss
1.	Stamlo-5	0.069	0.068	1.449%	1.84%
2.	Amlopres-5	0.12	0.11	8.33%	0.83%
3.	Amlopin	0.196	0.193	1.53%	0.82%
4.	Amlodac-5	0.067	0.066	1.492%	1.49%
5.	Amlokind-5	0.154	0.153	.0.649%	0.65%
6.	Amcard	0.0906	0.089	1.11%	1.77%

Discussion

From the above experimental data we conclude that Amlokind-5 was having the acceptable percent of friability i.e, 0.649%.

CONCLUSION

A comparative study of six different brands of Amlodipine (employed especially for the treatment of Hypertension and other Coronary artery disease like Angina pectoris) and their quantitative evaluation by UV Spectrophotometry was carried out. The six different brands of Amlodipine 5mg tablets(Amlokind-5,Amlopin,Amcard,Stamlo-5,Amlodac5,Amlopres-5) by six pharmaceutical companies (Mankind Pharma Ltd .,USV Ltd.,Systopic Lab Pvt Ltd.,Dr.Reddy's Lab Ltd.,Zydus Health Care,Cipla Ltd.) respectively were used. These brands were chosen because they are readily available in Indian market as well as because of their cost fidelity.The pharmaceutical equivalency of six different brands of Amlodipine 5mg tablets were assessed through the quantitative evaluation,weight variation est, friability test, disintegration test .In the current study methanol is used as solvent and the detection was carried out at a wavelength 237 nm in a UV Spectrophotometer .The calibration graph of standard amlodipine and six different brands of amlodipine was found to be linear in the concentration range of 10-60µg/ml with regression coefficient value of 0.98 .It was found that Weight Variation Test of Amlodac-5 and Stamlo-5 were not in the acceptance limits and the remaining four tablets passes the Weight Variation Test i.e., they lie within the acceptance limits of (±7.5). The percentage of friability for Amlokind-5 was found to be 0.649% which was less than 0.8% (normal limits) and the remaining brands were found out of limits with little variations. The disintegration time was found to be 10 seconds (Fastest release) for Amlopres-5 and 4.43 minutes (Slowest release)for Amlodac-5.The best tablet among all the six brands was Amlokind-5(Mankind Pharmaceuticals) as its concentration falls within the acceptable limits of Beer-Lamberts law(10-60µg/ml),and it also passes the Weight variation test (with limits±7.5),Disintegration test(with <20 seconds) and Friability test with 0.649%.Based on cost analysis data amlokind-5 has the lowest price of (Rs 33/-) which makes it cost effective and preferable in management of Hypertension. This method is simple, rapid and Economical. Hence it can be easily and conveniently adopted in routine lab analysis for Comparative Studies.

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