WORLD JOURNAL OF PHARMACEUTICAL RESEARCH
SJIF Impact Factor 8.453
Volume 13, Issue 11, 1044-1056. Research Article ISSN 2277–7105

FORMULATION AND EVALUATION OF IMMEDIATE RELEASE VALSARTAN TABLET

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Article Received on
05 April 2024,

Revised on 25 April 2024,
Accepted on 15 May 2024

DOI: 10.20959/wjpr202411-32381

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ABSTRACT

The immediate release tablet of antihypertensive drug valsartan were prepared evaluate to increase solubility and bioavability. Valsartan is an Angiotension II type I receptor antagonist indicated were prepared by direct compression method. Valsartan tablets were formulated by using microcrystalline cellulose, potato starch, acacia, magnesium stearate and sodium lauryl sulphate. The prepared valsartan immediate release tablets were evaluate for various parameters like weight variation, hardness friability, thickness, disintegration time, dissolution studies and assay. The blend was examined for the pre –compression and post compression parameter. The value of pre-compression parameter evaluates were within prescribed limit and indicates good flow property. All the post compression parameter are evaluated were prescribed limits and results were within IP acceptable limits. Based on the disintegration time and dissolution studies formulation F1 and F5 were found to be optimize and showed a disintegration time of 52 sec respectively.

INTRODUCTION

Tablets are solid unit dosage forms containing a single dose of one or more active ingredients and obtained by compressing uniform volumes of particles. They are intended for oral administration. Some are dissolved or dispersed in water before administration and some are retained in the mouth, where the active ingredients are liberated.

Advantages

- They are unit dosage form, and they offers the greatest capabilities of all oral dosage forms are the greatest dose precision and the least content variability.

- Their cost is lowest of all oral dosage form.
- They are the lightest and most compact of all oral dosage forms.

Disadvantages

- Some drugs resist compression into dense compacts, owing to their amorphous nature or flocculent, low density character.
- Drugs with poor wetting slow dissolution properties, intermediate to large dosage, optimum absorption high in the gastrointestinal tract, or any combination of this features may be difficult or impossible to formulate and manufacture as a tablet that will still provide adequate or full drug bioavailability.

Valsartan

Valsartan is usually considered the angiotensive II receptor antagonist of choice for anti-hypertensive effects. It is indicated in conditions where hypertension therapy is likely to be beneficial. Valsartan is a BCS class II drug having low solubility and high permeability.

Immediate release

Immediate release tablets are those which disintegrate rapidly and get dissolve to Release the medicaments. Immediate release may be provided for by way of an appropriate pharmaceutically acceptable are designed for immediate release of drug absorption.

AIM AND OBJECTIVE

Aim of this study is to **Formulation and evaluation of immediate release valsartan tablet** by direct compression method and evaluate the formulation for various pharmaceutical parameters.

The purpose of the present study the aspects of the formulation and the effects of different excipients during formulation and evaluation.

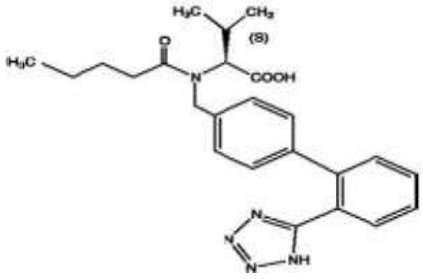
Drug profile

Valsartan sodium

Valsartan is an on peptide, orally active, and specific angiotensin II receptor blocker acting on the AT1 receptor subtype.

1. **Chemical name:** ValsartanischemicallydescribedasN-(1-oxopentyl) N-[[2'-(1H- tetrazol-5-yl) [1,1'-biphenyl]-4-yl]methyl]-L-valine.

2. **Molecular formula:** C24H29N5O3
3. **Molecularweight:** 435.5
4. **Chemical structure**



5. **Category:** Antihypertensive
6. **Appearance:** Valsartan is a white to practically white fine powder
7. **Solubility:** It is soluble in ethanol and methanol and slightly soluble in water.
8. **Melting point:** The melting point was found to be 102°C.
9. **Storage:** Store at 25°C Protect from moisture

MATERIALS AND METHODS

Calibrationcurveofvalsartan

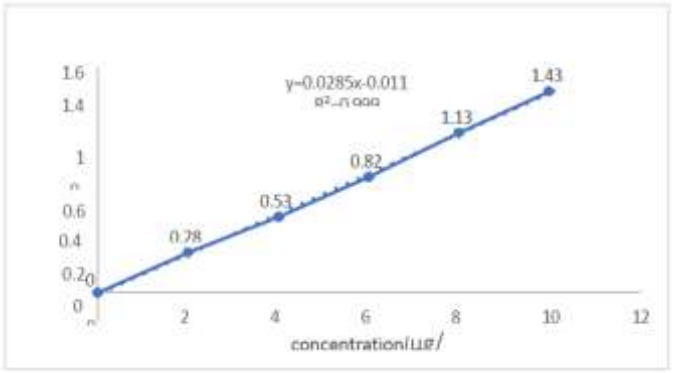
Preparation of 0.1N sodium hydroxide

4gm of 0.1N Sodium Hydroxide was taken an dissolved in1000ml of distilled water.

Preparation of Ph 6.8 Buffer (Phosphate buffer)

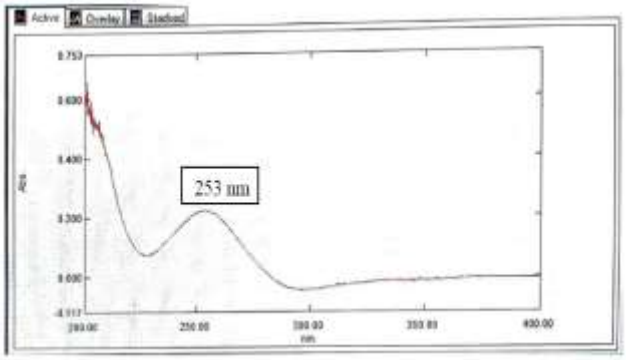
2.7218 gm of potassium dihydrogen ortho phosphate was dissolved in 100ml of distilled water. Then from the potassium dihydrogen ortho phosphate solution 25ml was taken and mixed with 11.2ml of 0.1N sodium hydroxide solution. Finally, make a 100ml by distilled water.

Preparation of standard curve of valsartan



10mg of Valsartan was accurately weighed and dissolved in small portion of phosphate buffer pH 6.8 in a 10ml volumetric flask and made up to 10ml with buffer. This is a primary stock solution. From the primary stock solution, 1ml was accurately pipette out and transferred into a 10ml volumetric flask. Then the volume was made up to 10ml with buffer. From the secondary stock solution aliquots equivalent to 2 -10 µg (1, 2, 3, 4, 5 ml) were pipetted out into a series of buffer. The absorbance of above set solution measured against phosphate buffer pH 6.8 as blank at 253 nm. Then calibration curve was plotted by taking concentration on X-axis and absorbance on Y-axis.

Concentration	Absorbance
2µg/ml	0.286
4µg/ml	0.539
6µg/ml	0.823
8µg/ml	1.136
10µg/ml	1.431



Formulation of valsartan tablets by direct compression method

Oro dispersible tablets of Valsartan were prepared by direct compression method.

Directcompression method

Sieving

The active ingredient was passed through the sieve #40. The other ingredients given in the formulation table were passed separately through the same sieve. Dry mixing all the materials (Including the active ingredient) were taken in polybag and mixed for10minutes.

Lubrication

The magnesium stearate was passed through the sieve#60 and mixed together the powder in a poly bag for 5 minutes to get a uniform blend.

Compression

Finally, the tablet blend was compressed into tablets by using16 stationrotary tablet press which contains punch size of 11mm in diameter.

Ingredients	F1	F2	F3	F4	F5
Valsartan	80mg	80mg	80mg	80mg	80mg
Micro crystalline cellulose	91mg	88 mg	86mg	84mg	82mg
Potato Starch	19mg	19mg	19mg	19mg	19mg
Acacia	4mg	4mg	4mg	4mg	4mg
Talc	2mg	2mg	2mg	2mg	2mg
Magnesium Sterate	4mg	4mg	4mg	4mg	4mg
Lactose	50mg	51 mg	52mg	53mg	54mg
Sucrose	50mg	52 mg	53mg	54mg	55mg
Total weight	300mg	300mg	300mg	300mg	300mg

Post compression parameters

The compressed tablets were evaluated for the following parameters.

General appearance

The tablet should be free from cracks, depressions, pin holes etc. The colour and polish of the tablets should be uniform on whole surface. The surface of the tablets should be smooth. The tablets were examined externally under a biconvex lens for surface cracks depression and pinholes.

Hardness test

The strength of a tablet to stand against applied load/ pressure is known as hardness. It is also known as crushing strength. Randomly take 5-10 tablets from prepared batch and hardness should be determined by crushing the tablet by hardness tester and then find out the average and standard deviation. Hardness is determined by using hardness tester (Monsanto).The value of hardness was calculated in kg/cm^2.

Thickness

Twenty tablets from the sample were randomly taken and individual tablet thickness was measured using digital Vernier calipher. Average thickness and standard deviation values were calculated. The thickness was denoted in mm.

Friability

Friability is to measure the extent of tablet breakage during physical stress conditions like packaging, transportation etc.Asampleofrandomlyselected6tabletswas evaluated for friability

using Roche friabilator at 25rpm for 4 minutes. The %weight loss is calculated by measuring the total weight of 6 tablets before and after operation. Formula for calculating the % weight loss is given below.

$$\%Friability = \frac{initial weight - final\ weight}{initial weight} \text{ X } 100$$

Weight variation test

To study weight variation, 20 tablets of each formulation were weighed using an electronic balance, average weights was calculated, individual tablet weights were compared with the average weight. Not more than two individual weights deviate from the average weight by more than the percentage deviation and none should deviate by more than twice that percentage.

$$\%\ Deviation = \frac{average\ weight - initial\ weight}{average\ weight} X100$$

Average weight of tablets (mg) in I. P	Percentage deviation
130orless	±10
130– 324	±7.5
Morethan324	±5

Disintegration test

Disintegration test was carried out at 37°C ± 2°C. Tablets were taken and introduced in each tube of disintegration apparatus, and the table track of the disintegration apparatus was positioned into a1litre beaker containing 900 ml of distilled water and the disc was not used for the study. The time taken for complete disintegration of the tablets with no palpable mass remaining in the apparatus was measured.

***Invitro*dissolutionstudies**

The *in vitro* dissolution studies of Valsartan IR tablets were performed using USP dissolution apparatus type1 (basket). The volume of dissolution medium (Phosphate buffer) used was 500ml and the temperature was maintained at 37°C±0.5°C. The speed of the basket was set at 50rpm. One tablet was placed in each jar of dissolution apparatus.5mlofsample from each jar was withdrawn at very 10 minutes interval lupto 90 minutes and same volume of 0.1M HCl was replaced to each dissolution jar, so that volume of dissolution medium was maintained to 500ml. Then the sample was filtered and diluted with Phosphate buffer and the amount of

Valsartan released from Immediate release tablets was determined spectrophotometrically at 255 nm using phosphate buffer as blank.

Assay

Ten tablets from each batch were weighed and finely powdered. Powder equivalent to 80 mg of Valsartan was dissolved in100ml of phosphate buffer pH6.8 and he solution was filtered by using Whatmanfilter paper and then further 0.8ml from this solution were diluted up to 10 ml with phosphate buffer in a 10 ml volumetric flask. The solution was analyzed for drug content at 255 nm using UV visible spectrophotometer.

RESULTS AND DISCUSSION

The present study was undertaken to formulate **Valsartan** by direct compression method using various excipients such as MCC, potato starch, acacia, Talc, magnesium stearate DCV. Totally five formulations (F-I to F-V) were prepared. The prepared blend of differentformulationsareevaluatedforpre-compressionparametersandtheprepared tablets of various formulation are evaluated for post compression parameters. The results are presented as following relevant tables and figures.

Preformulation studies

Organoleptic properties

The organoleptic properties of Valsartan (API) was given in the below table.

Table: Organoleptic properties of valsartan (API).

Tests	Specifications	Observation
Colour	White	White
Odour	Odourless	Odourless
Taste	Bitter	Bitter

The organoleptic properties of the Valsartan (API) like colour, odour and taste were evaluated. The study reveals that the Valsartan shows similar colour, odour and taste as per I.P specification.

Solubilitytest

The solubility profile of the Valsartan (API) was given in the below table,

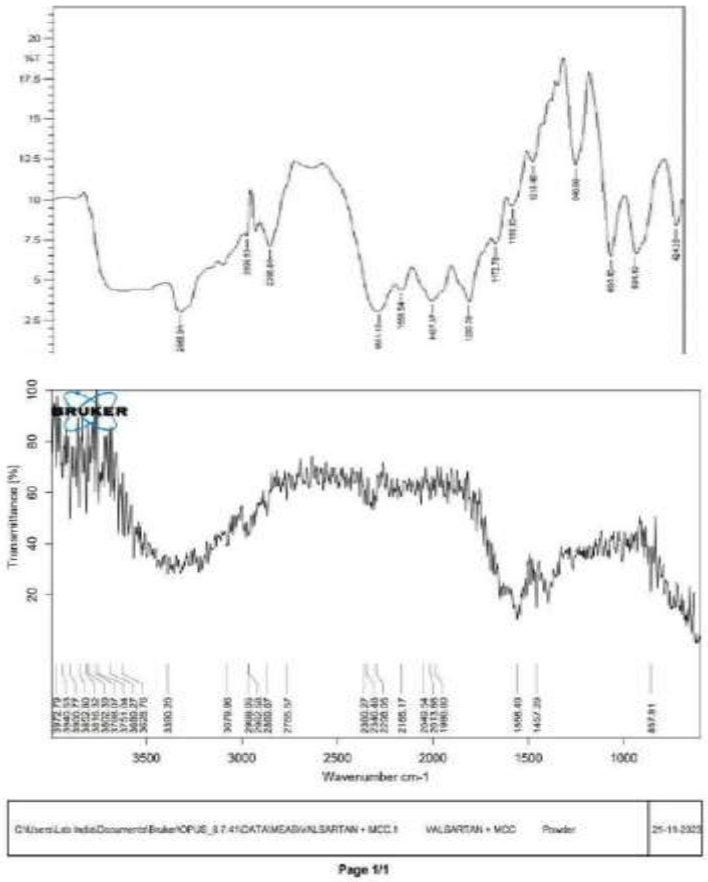
Table: Solubility profile of Valsartan

Valsartan(API)	Solubility
Valsartan	Free soluble in water, Soluble in methanol and Insoluble in dicholoromethane.

The solubility studies of the Valsartan (API) revealedthatthedrug was Freely soluble in water Soluble in methanol and insoluble in dicholoromethane.

FT-IR spectral studies

The FT-IR studies are carried out for pure Valsartan raw material and Valsartan with MCC were carried out to find any interaction between drug and excipient used in the formulation. The study was carried out by IR Spectroscopy (SHIMADZU).



Interpretation

Types of bond	Wave number
O-H stretching	3390.20cm^{-1}
C-H Stretching	3079.96cm^{-1}
C-O Stretching	1250cm^{-1}
C-C Stretching	1558.49cm^{-1}

The FT-IR spectral studies shows that the drug is compatible with all the excipients. The FT-IR spectrum of physical mixture shows all the characteristic peaks of Valsartan, thus confirming that no interaction of drug occurred with the components of the formulation.

Pre-compression parameters

micromeritic properties

The powder blends are evaluated for the micromeritic properties such as angle of repose bulk density, tapped density, compressibility index and Hausner's ratio. The results are given in the below table.

Table: Pre compression parameters.

Formulation Code	Angle of Repose	Bulk Density g/cm3	Tapped Density g/cm3	Compressibility Index (%)	Hausner's Ratio
F I	37.2	0.461	0.682	20.01	1.210
FII	35.3	0.459	0.573	19.05	1.235
FIII	40.3	0.456	0.488	18.04	1.211
FIV	33.1	0.440	0.685	19.04	1.234
FV	35.4	0.438	0.574	18.03	1.239

The angle of repose of Formulation I was found to be 25º31' which indicates excellent flow property and the angle of repose of other formulations was found between 25º09'and 27º74'which indicates excellent flow property. The bulk density was found to be between 0.3170 to 0.3173 g/cm3, the tapped density was found to be between 0.3840 to 0.4410 g/cm3, the compressibility index was found in the range of 17.40 to 19.04% and the Hausner's ratio lies between 1.210 to 1.235. The above results in the term of micromeritic properties reveals that the flow property of the Formulation-I was good and other was fair.

Post compression parameters

Table: Post compression parameters.

Formulation Code	Thickness (mm)	Hardness (kg/cm2)	Weight Variation (mg)	Friability (%)
F I	4.026±0.0152	5.00±0.37	300.02±3.66	0.68
FII	4.023±0.0152	4.57±0.25	295.11±4.85	0.63
FIII	4.020±0.010	4.92±0.33	296.17±4.69	0.65
FIV	4.023±0.015	4.45±0.38	297.11±3.71	0.66
FV	4.022±0,014	4.46±0.3	298±3.46	0.67

All the values are expressed as mean ± SD, n=3

The thickness of the tablets was measured and it was found in the range between

4.023±0.0152 and 4.026±0.015 mm. All the formulations are under uniform thickness.

The hardness of the tablets was measured and it was found in the range between 4.45±0.38and 5.00±0.37 kg/cm^{2}and the tablets possess good mechanical strength and sufficient hardness.

All the formulations of the Valsartan IR tablets passed the weight variation test and the values are within the acceptable limit.

The friability percentage values of the Valsartan IR tablets shows less than 1% weight loss and is within the limit. Hence all the tablets passed the friability test.

Evaluation of valsartan ir tablets

Table 18: Evaluation of valsartan tablets.

Formulation code	Disintegration test (Sec)
F1	12±1.52
F2	30±2.08
F3	15±2.51
F4	13±1.52
F5	12±1.52

All the values are expressed as mean ± SD, n=3

Disintegration time of Valsartan tablets ranges between 12 to 30 seconds. As per I.P the disintegration time limit is 30seconds. Our Formulation I shows least disintegration time (12 sec) compared with other formulations.

Assay of valsartan by uv spectroscopy method

The assay of Valsartan tablets was done by UV spectroscopy method as per the procedure given in the methodology. The assay values of the Valsartan IR tablets are given in the below table.

Table 19: Assay of Valsartan IR tablets by UV Spectroscopy.

Formulation Code	Limit (%)	Assay (%)
F I	98to102%	99.29%
FII		98.28%
FIII		95.00%
FIV		94.25%
FV		95.65%

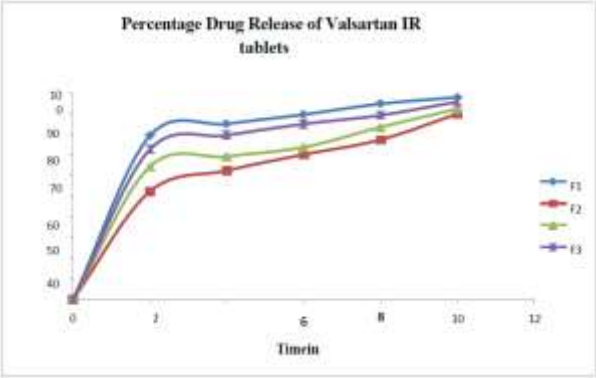
The assay of Valsartan IR tablets were found in the range between 94.25% and 99.29%. As

per I.P the acceptable limit of the Valsartan IR tablets is 90 to 110%. The above results revealed that the assay of Valsartan IR was within the acceptable limits.

***In vitro* dissolution studies**

Table 20: The *In Vitro* drug release of the Valsartan IR tablets.

Time in minutes	Percentage Drug Release (%)				
	Formulation Code				
	FI	FII	FIII	FIV	FV
2	79.41±1.91	52.32±0.87	64.46±1.01	72.75±1.76	73.74±1.75
4	85.05±1.90	62.43±0.71	69.30±0.68	79.54±1.21	77.54±1.21
6	89.62±2.77	70.21±2.91	73.78±1.75	85.05±1.79	89.05±1.75
8	94.80±1.81	77.40±2.69	83.54±1.71	89.32±3.01	88.32±3.02
10	98.00±2.08	90.00±1.52	92.42±1.47	95.85±2.03	97.85±2.03



The release of Valsartan IR tablets was studied in phosphate buffer 6.8 upto 90minutes.The formulation F-1orF-5 at different concentration of Microcrystalline cellulose are preferred Immediate release tablets best form F-5.

The drug release of formulation F-I, F-II, F-III, F-IV, F-V was found to be 98.00±2.08%, 90.00±1.52%, 92.42±1.47%, 95.85±2.03%, 97.85±2.03 at 10 minutes. The acceptable limit of *in vitro* dissolution is NLT 80% of drug release at 10minutes.All the formulations are passed the in vitro dissolution studies. The higher dissution rates were observed in F-I and F-V using Magnesium stearate and DCV as excipients due to rapid disintegration and fine dispersion of particles after disintegration.

SUMMARY AND CONCLUSION

The present study was undertaken to formulate Valsartan IR Tablets by direct compression method using various excipients such as Magnesium stearate, MCC, Potato starch, acacia, Talc and DCV. A total of four formulations(F-I to F-V) of Valsartan IR tablets were prepared

by direct compression method. All the formulations were evaluated for both precompression and post compression parameters as per the requirements of standards. Pre formulation study of API such as organoleptic properties, solubility, compatibility study and FT- IR drug - excipients interaction study were carried out. The prepared blends were also evaluated for pre compression parameters such as angle of repose, bulk density, tapped density, compressibility index and hausner's ratio. The prepared tablets were evaluated for post compression parameters such as thickness, hardness, weight variation, friability, disintegration, wetting time, water absorption ratio, taste evaluation, assay and *invitro* drug.

From this study, the overall results revealed that the Formulation F-I and F-V contains Magnesium stearate and DCV as excipients gives better results when compared to other formulations. Despite that, Magnesium stearate which gives maximum drug release.

The work concluded that the Valsartan IR tablets could be successfully formulated by direct compression method using various excipients insame concentration.

The Formulation F-I which contains Magnesium stearate may enhance the dissolution rate, provides convenience administration, patient compliance and therapeutic effectiveness.

From the above observation, it was concluded that the Formulation F-I containing Magnesium stearate was found to be better one compared to the other formulations.

REFERENCES

1. Robinson JR, Lee VHL. Controlled Drug Delivery: Fundamentalsand Applications, New York, Marcel Dekker, Inc, 1987; 2.
2. Rastogi V, Pragya PU. A brief view on antihypertensive drugs delivery through transdermal patches. International Journal of Pharmaceutical Sciences and Research, 2012; 1, 3(7): 1955.
3. S. Indumathy and KavimaniS Anti Inflammatory Activity of Angiotensin Antagonists Pharmacie Globale© (IJCP), 02, 01: 1-2.
4. S.P. Vyas and Roop K. Khar., Controlled Drug Delivery, Concepts and advances, Vallabh prakashan, 97-111.
5. Zaid AN, Ghanem M, Shweiki DA, Shtewi H, Shaheen R, Al Helaly S, Khayyat Z, Al Ramahi RA, ZyoudSE. Invitroandinvivopostmarketingsurveillanceofvalsartan, alone or in combination with amlodipine or hydrochlorothiazide, among Palestinian

hypertensivepatients. Therapeutics and clinicalriskmanagement, 2016; 19: 1425-32.

6. Leon Shargel, Susanna Wu-Pong, Andrew BC Yu. Modified-release drug products. In: Applied Biopharmaceutics & Pharmacokinetics, 2004; 5.
7. Mahajan P, Mahajan SC, Mishra DK. Valsartan release from sustained release matrix tablet and effect of cellulose derivatives. Int J Pharm Sci, 2011; 2: 521-30.
8. Chinam Niranjan Patra An overview of controlled-release systems. In: wise DL. ed, Handbook of Pharmaceutical Controlled Release Technology, Marcel Dekker, 2000.
9. D. Srinivas, Subal Debnath, T.R.S Chowdary, S.Y. Manjunath Formulation and evaluation of Valsartan film coated tablets J. Chem. Pharm. Res, 2011; 2(5): 534-540.
10. Deshpande MM, Mahajan MP, Sawant SD. Simultaneous estimation of valsartan and hydrochlorothiazide in fixed dose combination in UV spectrophotometry. International Journal of pharmaceutical sciences and Research, 2012; 1, 3(1): 236.
11. DM Brahmankar and SB Jaiswal, Biopharmaceutics and Pharmacokinetics, Vallabh Prakashan, 1995; 337.
12. G. Nicholas Sustained release dosage forms. In: Leon Lachman, Herbert A. Liberman, Joseph LK. The Theory and Practice of Industrial Pharmacy. Varghese Publishing House, Bombay, 1987; 3: 430-456.