PHARMACEUTICAL AND BIOLOGICAL EVALUATION OF BRANDS OF ALBENDAZOLE TABLETS ON THE GHANAIAN MARKET.

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DECLARATION

The experimental work described in this thesis was carried out at the Department of Pharmaceutical Chemistry, KNUST. This work has not been submitted for any other degree.

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ABSTRACT

The dissolution characteristics of the various brands of **albendazole** have long been a problem to manufacturers. Since dissolution affects the bioavailability of drugs, it is important that all steps be taken to solve this problem once and for all. The possible reasons for the problematic dissolution profile of albendazole are differences in manufacturing processes, compression pressures, levels of excipients particularly, binders, diluents, crystal size and structure of albendazole granules used for compression etc.

The effect of chewing on the dissolution was also investigated.

The effect of the sparing solubilities and erratic dissolution profiles of albendazole was investigated by their activity on the mobility of earth worms *(Lumbricus terretis*). A simple analytical method was developed for the assay of albendazole using high performance liquid chromatography (HPLC). A solvent system of 200 volumes of water, 800 volumes of methanol with 3ml of sulphuric acid in methanol was used. The chromatographic system was equipped with a 254nm detector and C18 column. The method developed was found to be specific, precise, accurate and linear. The method was also robust, flow rates of 0.5ml/min and 1.0ml/min were recommended. The limit of detection (LOD) and limit of quantification (LOQ) were respectively 24ug/ml and 80ug/ml.

The following brands of albendazole were used: *zentel, tanzol, alben, wormplex, wormzap, albendaven, expel, nesben, and benzil.*

Upon investigation, chewing a tablet of albendazole improves drastically its dissolution and efficacy. It is therefore advised that all albendazole tablets be chewed before swallowing.

All the brands of albendazole effectively killed the worms after three hours of experimentation. The differences in paralysis time were investigated by chemical assay. The purpose of the chemical assay (via non-aqueous titration and HPLC) was based on the premise that

differences in the active ingredient content could contribute to the difference in the paralysis time.

Using non-aqueous titration, only sample K was found to contain the appropriate amount of albendazole by virtue of its % active ingredient content. However, using HPLC samples K, B, C, D and A contained the appropriate amount of active ingredient using the British Pharmacopoeia (BP), United States Pharmacopoeia (USP) and the International Pharmacopoeia (IP) as references.

The two methods employed revealed the sensitivity, accuracy and reliability of HPLC over non-aqueous titration, in the analysis of albendazole.

The differences in the % active ingredient content contributed to the effects of tablets on the paralysis of the worms, hence playing a crucial role. This was demonstrated by the paralysis activities of samples A, B and C over the other brands.

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ABBREVIATIONS

BP:	British Pharmacopoeia
USP:	United States Pharmacopoeia
IP:	International Pharmacopoeia
HPLC:	High Performance Liquid Chromatography
TLC:	Thin Layer Chromatography
ODS:	Octadecyl silane
Rf:	Retention factor
FDA:	Food and Drugs Authority
EU:	European Union
GMP:	Good Manufacturing Practices
LOD:	Limit of Detection
LOQ:	Limit of quantification
U.V:	Ultra-violet
NADH:	Reduced nicotinamide-adenine dinucleotide
RSD:	Relative Standard Deviation
S.D:	Standard Deviation
R	Reagent grade chemical
RS	Reference standard

Chapter 1

INTRODUCTION

1.1 GENERAL INTRODUCTION

Quality assurance of drugs in third world countries is an often neglected issue. Sometimes lack of quality assurance can lead to dire consequences, resulting in incidences such as the Haiti tragedy, where children died from contaminated acetaminophen syrup.

In addition to the content and purity of a drug formulation, its ability to release the required amount of the drug within a certain time is an important factor in drug product quality. Especially for drugs with low solubility, the release characteristics of the dosage form play an important role in the availability of a drug, either in terms of its systemic availability or where appropriate, for its local action in the gastrointestinal tract. The quality of excipients used (binders, lubricants, disintegrants, surfactants) in the manufacturing and the quality of the process itself is consequently of great importance to the performance of formulations of poorly soluble drugs.

The drug under investigation, **albendazole,** an *anthelmintic* has weak basic properties, and an aqueous solubility of approximately 1microgram/ml.

Drugs like **albendazole** exhibit problematic dissolution characteristics. Reproducible and sufficient release of these compounds can only be guaranteed by careful formulation and high quality manufacturing procedures[1].

A common approach taken to improve the release rate of poorly soluble drugs is to increase the available surface area of drug for dissolution, either by increasing the surface area by means of micronization or by adding surfactants to the formulation.

1.1 OBJECTIVES

The objectives of the work are as follows:

- To identify the brands of albendazole using infrared spectroscopy

- To perform preliminary tablet tests (using BP and non-BP methods)
- To perform dissolution test for whole and crushed tablets
- To assay the tablets using non-aqueous titration and high performance liquid chromatography
- To perform a biological assay of the tablets using earth worms
- To statistically analyse the results of method validation

LITERATURE REVIEW

1.2 IDENTIFICATION

Identification of the test sample is one important preliminary test that needs to be carried out. The identity of the sample under test needs to be ascertained before further experimental work could be done. The identification of the state of purity of the pure sample is also of prime importance.

Two methods were used to identify the purity of the pure sample;

- Infrared spectroscopy
- Thin-layer chromatography

1.2.1 Infrared spectroscopy

Infrared spectroscopy determines the absorption recorded by the samples under the infrared portion of the electromagnetic spectrum.Vibrational frequencies registered by the various functional groups (usually very characteristic) are recorded as spectra.

1.2.2 Thin Layer Chromatography

Thin-layer chromatography is a separation technique in which a stationary phase consisting of an appropriate material is spread as a uniform thin layer on a support of glass, metal or plastic. The separation is based on adsorption, partition, ion-exchange or on combinations of these mechanisms. The separation is carried out by migration of solutes in a solvent or a suitable mixture of solvents (mobile phase) through the thin-layer (stationary phase). When a mixture of analytes is spotted and dried on the plates, the drugs move across the plate at different rates

depending on the extent of adsorption or partitioning on the plates and its solubility in the mobile phase.[2]

Some of the stationary phases used for TLC include Silica gel, cellulose, Alumina (aluminum oxide), magnesium silicate, ion exchange resins and reversed phases like paraffin and octadecyl silane, ODS.

TLC is one of the most widely used techniques for the separation of pharmaceutical products and their identification. This method of characterization has gained popularity and favor as an analytical method because of its simplicity, reliability as well as the simple method location procedures.

1.2.3 Location of spots

As most organic compounds are colourless, they must be made visible, preferably by a non destructive technique. Most compounds can be located by examining plate containing a chromophore under a 254nm wavelength. In this process the absorbing compounds are seen as dark spots. These spots can be ringed up with a pencil. Compounds that naturally fluoresce can be located under uv lamp as coloured spots. Another very important but destructive test is to spray ethanolic sulphuric acid on the plate and gently warm in an oven. Organic material when treated in such manner, char-up and are seen as dark spots.

1.2.4 Retention Factor (Rf)

The basic chromatographic measurement of a substance on TLC is the Retention factor (Rf). The distance travelled by the substance is measured from the centre of the round spot. However if the spot is tailing, it is measured from the middle of the dense area of that spot. Rf values needed for the identification of samples are to be run at the same time and on the same

plate with both known and unknown side by side. The Rf value if quoted as a fraction ranges between 0 to 1 and if quoted as a percentage ranges between o to 100. [3]

$$R_f = \left(\frac{Distance\ \ travelled\ \ by\ solute\ \ from\ \ origin}{Distance\ \ travelled\ \ by\ solvent\ \ from\ \ origin} \right)$$

1.3 Theory and instrumentation of analytical methods

1.3.1 High performance liquid chromatography (HPLC)

HPLC is now the most widely used method of assay and separation technique. The simple high performance liquid chromatographic method developed in the late 1960s has evolved into high pressure and high speed chromatography. HPLC has many advantages over the classical column chromatography. With the packed stationary phase made of smaller particle size, there are improved resolution of substances, faster separation with increased precision and accuracy. The separation principles used for effective separation involves adsorption, partition, ion exchange and gel permeation.[4]

1.3.2 Instrumentation

The basic instruments consist of mobile phase reservoir, a high–pressure pump, an injector, a stationary phase embedded in a stainless steel column, a detector and a chart recorder.

1.3.3 High Pressure Pumps

High pressure pumps are an important part needed to deliver a constant flow of the mobile phase with a decisive pressure. Most pumps are able to deliver a constant pressure range of -600bar. A dual – Piston reciprocating pump is performed due to its pulse-free flow. In this

system as one shaft phase is filling the valve another phase is pumping the mobile phase. Unlike a single piston pump a damping device is required to smoothen out the flow. This is necessary so as to avoid excessive noise at high level of sensitivity causing high base line noise preventing small quantities of substances to be detected. [2]

1.3.4 Injector system

The sample solution is introduced into the flowing mobile phase at or near the head of the column using an injection system which can operate at high pressure. They contain Fixed- loop and variable volume devices which are operated manually or by an auto-sampler are used. Manual partial filling of loops may lead to poorer injection volume precision. The sample is introduced into the loop when the valve is in the load position. At this stage the eluent flows from the pump to the column through another passage. When the valve is switched to inject, the loop is redirected to flow into the column conveying the sample into its destination.[2]

1.3.5 Column

The columns are made of highly polished stainless steel usually having a column length of 10 to 30cm and an internal diameter of 4.5 to 5mm. Longer and larger pore size columns are available and are used usually for commercial purposes.

The most widely used stationary phase is silica ($SiO_2.XH_2O$). The stationary phase consists of a network of siloxane linkages (Si-O-Si) in a rigid three dimensional structure containing interconnecting pores. The pore size and the amount of silanol groups are controlled in the manufacturing process.

In a straight stationary phase column the silanol groups are vital as they are involved in adsorption chromatography.

Silica can be modified to the reversed stationary phase. This is done by a controlled reaction of organochlorosilanes with the silanol groups or the use of organoalkoxysilanes which modifies

the surface of the silica. The linkage of these hydrocarbons to the surface impacts a non polarity to the surface and enhances partitioning, thus the separation of lipophilic compounds.

The most popular stationary phase material used is the (ODS) Octadecyl-silica C18.Others include, octyl (C_8), Phenyl (C_6H_5), Cyanopropyl ($(CH_2)_3$-CN) and aminopropyl ($(CH_2)_3$-NH_2) groups.

Pharmaceutical products contain both lipophilic and polar groups. These groups are exploited during separation on columns. [5]

1.3.6 Detectors

Four main types of detectors are frequently used in High performance liquid chromatography. These are the electrochemical detectors, Fluorescent detector, Refractive index detector, Mass spectrometers, Radioactivity detectors and the Ultra-Violet visible detectors. Among these, the most widely used is the Ultra-Violet Visible detectors.

1.4 Method Validation

Validation under the food and Drugs Authority (FDA) guidelines is defined as establishing documented evidence which provides a high degree of assurance that a specific process will consistently produce a product meeting its pre-determined specifications and quality attributes.

Under the European (EU) guidelines, validation is defined as the action of proving, in accordance with good manufacturing (GMP) principles that any procedure, process, equipment, material, activity or system actually leads to the expected results**.**

Method validation is the process of demonstrating that analytical procedures are suitable for their intended use.

1.5 Validation Parameters

1.5.1 Specificity

This is the ability to assess unequivocally the analyte in the presence of components which may be expected to be present (impurities, degradants, matrix). Therefore it is the ability of a method to discriminate between the intended analyte(s) and other components in the sample. Specificity of the HPLC method is demonstrated by the separation of the analytes from other potential components such as impurities, degradants or excipients. In addition, stressed samples under forced degradation conditions (acid, base, heat, moisture, light, and oxidation) are used to challenge the method. If a placebo is not available, non-interference from contaminants and reagents is demonstrated by running a procedural blank.

1.5.2 Linearity

This is defined as the ability (within a specified range) to obtain test results which are directly proportional to the concentration of analyte in the sample. In HPLC methods, the relationship between detector response (peak area or height) and sample concentration (or amount) is used to make this determination. Evaluation of linearity is by visual inspection of the plot and by statistical techniques. Calculation of correlation coefficient, y-intercept, slope etc is of significance as far as the parameter is concerned.

1.5.3 Accuracy

This expresses the closeness of agreement between the value which is accepted either as a conventional true value or an accepted reference value and the value found. Accuracy studies are usually evaluated by determining the recovery of a spiked sample of the analyte into the matrix of the sample (a placebo) or by comparison of the result to a reference standard of known purity. If a placebo is not available, the technique of standard addition is used.[6]

1.5.4 Precision

This is the closeness between a series of measurements obtained from multiple sampling of the same homogeneous sample. Precision is a measure of the ability of the method to generate reproducible results. The precision of a method is evaluated for repeatability, intermediate precision and reproducibility.[6]

Repeatability is a measure of the ability of the method to generate similar results for multiple preparations of the same homogenous sample by one analyst using the same instrument in a short duration (e.g. on the same day).

Intermediate precision, synonymous with the term "ruggedness" , is a measure of the variability of the method results where samples are tested and compared using different analysts, different equipment, and on different days etc. This study is a measure of the intra-laboratory variability and is a measure of the precision that can be expected within a laboratory.

Reproducibility is the precision obtained when samples are prepared and compared between different testing sites. Method reproducibility is often assessed during collaborative studies at the time of technology or method transfer (e.g. from a research facility to quality control of a manufacturing plant).

1.5.5 Limit of detection (LOD)

LOD is the smallest amount or concentration of analyte that can be detected. There a number of ways for the calculation of LOD. The simplest method to calculate LOD is to determine the amount (or concentration) of an analyte that yields a peak with a signal-to-noise ratio of 2. [6]

1.5.6 Limit of quantitation (LOQ)

LOQ is the lowest concentration of an analyte that can be quantified with some degree of certainty (e.g. with a precision of 5%). The simplest method for calculating LOQ is to determine the amount (or concentration) of an analyte that yields a peak with a signal-to-noise ratio of 10. Thus LOQ is roughly equal to 3 times of LOD. [6]

1.6 UV visible Spectrophotometric analysis

The technique of Ultraviolet- visible spectrophotometry is one of the most frequently employed technology employed in pharmaceutical analysis. The wavelength used ranges from 190 nm – 380 nm for ultraviolet radiation and 380 nm–800 nm for visible radiation.[4]

Different sources of light are needed for the generation of the radiation needed. Hydrogen discharge lamps and xenon arc lamps are needed for ultraviolet radiation generation, and tungsten filament lamps and deuterium discharge lamps generate the radiation in the visible region. Since these light sources generate large range of wavelengths, there are monochromator filters incorporated in the machine that is able to filter and produce light of specified range of wavelength needed by the user. Examples of monochromator include prisms and diffraction gratings.

Light from the monochomator passes through the couvette containing the sample to the light detector system. The signals generated are compared with the incident light and the amount of light absorbed displayed by the machine.

The Beer-Lambert law is the basis for all analytical absorption spectrophotometry.

The law states that, the absorbance of a solution of a substance is related to the path length of the solution through which the light passes and to its concentration.[4, 5].

Mathematically: A= a*b*c

A = Absorbance

a= specific absorbance if concentration is in %w/v

b= Path length in cm

c= concentration in %w/v

Or

$A = \varepsilon bc$

A= Absorbance

ε = molar extinction coefficient

b = Path-length in cm

c = concentration in g/L

The law holds when monochromatic light is used and the solution used is diluted and stray light is excluded. Therefore, the plot of absorbance against varying concentration for a cell of unit thickness, usually 1cm should give a straight line passing through the origin. This is termed the calibration curve. The calibration curve can be used for the determination of the concentration of an unknown sample when the absorbance has been determined.

However, for a solution containing a mixture of compounds with each having a different maximum absorbance with spectral overlaps, the overall absorbance at their maximum wavelength will be equal to the summation of the specific absorbance of their product times the concentration.

1.7 Non-Aqueous Titrations[7]

1.7.1 Introduction

Substances which are too weakly basic or too weakly acidic to give sharp end-points in aqueous solution can often be titrated in non-aqueous solvents. Acetic acid is amphiprotic solvent. It dissociates to a small extent:

$CH_3COOH \rightleftharpoons H^+ + CH_3COO^-$

Here it is an acid. When a very strong acid such as perchloric acid is dissolved in acetic acid, the latter functions as a base:

$HClO_4 \rightleftharpoons H^+ + ClO_4^-$

$CH_3COOH + H^+ \rightleftharpoons CH_3COOH_2^+$ (onium ion)

Since onium ion readily donates its proton to a base, a solution of perchloric acid in glacial acetic acid functions as a strongly acidic solution.
The basic properties of a weak base are enhanced in acetic acid solution:

$R_3N + CH_3COOH \rightleftharpoons R_3N^+H + CH_3COO^-$

$CH_3COOH_2^+ + CH_3COO- \rightleftharpoons 2CH_3COOH$

Hence $HClO_4 + R_3N \rightleftharpoons R_3N^+H + ClO_4^-$

Perchloric acid prepared for the titration needs to be standardized, using potassium hydrogen phthalate (a primary standard).

Equation of standardization reaction

$HClO_4$ +

Definition of term

1.7.2 Primary standard

By direct weighing of a primary standard and dissolution in a known volume of water, a standard solution is obtained.[8]

1.7.3 Properties of a primary standard

A primary standard should as far as possible meet the following requirements:

1. It should be readily available in highly purified form
2. It should not be wetable in air at ordinary and fairly high temperature
3. It should have high equivalent weigh (this will reduce the effects of small weighing errors)
4. It should be readily soluble in the chosen solvent under the analytical conditions
5. It should give no interfering products during titration.

Examples of primary standard include sodium carbonate, potassium hydrogen phthalate, sulphamic acid etc.

1.8 PHARMACOPOEIAL AND NON-PHARMACOPOEIAL TESTS

1.8.1 Uniformity of Weight test

Standard of uniformity of weight is applied to tablets and capsules which are supplied in unit-dose forms and uniformity of volume to single dose pro-injections because they are subject to more variation than comparable preparations supplied in multi-dose forms.

As stated in the pharmacopoeia when twenty tablets are selected at random and a uniformity test performed, not more than two tablets should deviate from the average weight by a greater percentage as illustrated below and not even one should deviate by twice that value.

Mass range	Permissible % deviation
< 80mg	± 10
80mg-250mg	± 7.5
>250mg	± 5

1.8.2 Hardness & Friability

The resistance of tablets to abrasion, shipping, or breakage under storage conditions, transportation and handling before usage depends on its hardness. Quantitatively, hardness of tablet is determined either in N (Newton) or kg. The minimum satisfactory value for tablet hardness is 4kg or 40N. Hardness determination is made throughout the tablets' manufacturing to determine the need for pressure adjustment in the tabletting machine. The degree of hardness affects the dissolution of the tablet; hence, the hardness needs to be controlled. Another indicator for hardness is the friability. Under friability rather than measuring the force required to crash the tablet, the instrument is used to evaluate the ability of the tablet to withstand abrasion in packaging, handling and shipping. A number of tablets are weighed and placed in the friabilator and the machine allowed to operate for 4minutes at a total of 100 revolutions. For tablets with a unit mass equal to or less than 650 mg, a sample of whole tablets corresponding as near as possible to 6.5 g is used. For those higher than 650 mg, 10 whole tablets are used. A maximum loss of mass obtained from a single test not greater than 1.0 percent is considered acceptable for most products.

1.8.3 Disintegration and Dissolution

Dissolution of tablet is used to study the rate of dissolution of tablet following compendia parameters. Disintegration time determination is a useful tool in product control. However, disintegration of tablet does not imply the availability for absorption. A drug can have a rapid disintegration time but it does not mean the drug is biologically available. The dissolution rate of the drug from the primary particles of the tablet is an important factor in drug absorption and for many formulations it is the rate limiting step.

Dissolution usually involves a dissolution tank containing dissolution bowls and paddles with dissolution medium volume usually 900ml .The number of unit test include the use of 6 unit bowls. The standardized USP criteria for published tests using either the basket or the paddle are that, for each unit tested, not less than 70% of the active ingredient or ingredients dissolve within 30 minutes. If one unit fails to meet this requirement, a retest may be carried out using the same number of units.

1.8.4 Active ingredient content

The content of the active substance is of significance to the analyst. The presence of the active ingredient and also in the right amount determines the efficacy of the drug. Determination of active ingredient content of any drug formulation is also crucial in eliminating substandard and counterfeit drugs. Two methods were employed to determine the active ingredient content in the various brands of tablets:

1. Non-aqueous titration
2. HPLC(High performance liquid chromatography)

The following constitute the range of acceptable content of the active ingredient by their respective authorities:

BP: Albendazole contains not less than 98.0%and not more than the equivalent of 102.0%

IP: Albendazole contains not less than **98.0%** and not more than **101.0%** of $C_{12}H_{15}N_3O_2S$, calculated with reference to the dried substance

USP: Albendazole contains not less than 90.0% and not more than 110.0% of the specified amount

ALBENDAZOLE

Albendazole, marketed under a lot of names as *Albenza, Eskazole, or Zentel*, is a member of the benzimidazole compounds used as a drug indicated for the treatment of a variety of worm infestations. Although the use of albendazole for the treatment of worm infestations in the US is widespread, FDA has not approved it.

Albendazole is effective against

- Threadworms or pinworms
- Roundworms,
- Whipworms
- Tapeworms
- Hookworms

MODE OF ACTION

Vermicidal: Albendazole ($C_{12}H_{15}N_3O_2S$) causes degenerative alterations in the tegument and intestinal cells of the worm by binding to the colchicine-sensitive site of tubulin, thus inhibiting its polymerization or assembly into microtubules. The loss of the cytoplasmic microtubules leads to impaired uptake of glucose by the larval and adult stages of the susceptible parasites, and depletes their glycogen stores. Degenerative changes in the endoplasmic reticulum, the mitochondria of the germinal layer, and the subsequent release of lysosomes result in decreased production of adenosine triphosphate (ATP), which is the energy required for the survival of the helminth. Due to diminished energy production, the parasite is immobilized and eventually dies.

Albendazole also has been shown to inhibit the enzyme fumarate reductase, which is helminth-specific. This action may be considered secondary to the effect on the microtubules due to the decreased absorption of glucose. This action occurs in the presence of reduced amounts of nicotinamide-adenine dinucleotide in reduced form (NADH), which is a coenzyme involved in many cellular oxidation-reduction reactions.

Albendazole has larvicidal effects in necatoriasis and ovicidal effects in ascariasis, ancylostomiasis, and trichuriasis.[9, 10]

DOSAGE

Hydatid disease:

- Patients 60 kg or greater: 400 mg twice daily, with meals.
- Patients less than 60 kg: 15 mg/kg/day given in divided doses twice daily with meals (maximum total daily dose 800 mg).
- Treatment interval: 28-day cycle followed by a 14-day albendazole-free interval, for a total of 3 cycles.

NOTE: When administering albendazole in the pre- or post-surgical setting, optimal killing of cyst contents is achieved when 3 courses of therapy have been given.

Neurocysticerosis:

- Patients 60 kg or greater: 400 mg twice daily, with meals.
- Patients less than 60 kg: 15 mg/kg/day given in divided doses twice daily with meals (maximum total daily dose 800 mg).
- Treatment interval: 8-30 days.

SIDE EFFECTS

This medication may cause

- Dizziness, headache, fever, nausea, vomiting, or temporary hair loss.

In rare cases it may cause persistent sore throat, severe headache, seizures, vision problems, yellowing eyes or skin, dark urine, stomach pain, easy bruising, mental/mood changes, very stiff neck, change in amount of urine. Allergic reactions are also possible.

CONTRAINDICATION

- Hypersensitivity to the benzimidazole class of compounds.

Pregnancy class

Do not take when pregnant, and do not become pregnant for one month after taking this drug

MONOGRAPH OF ALBENDAZOLE[2, 12]

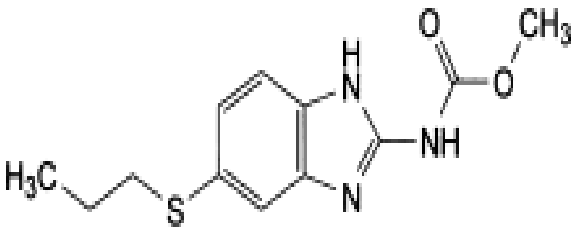


Figure 1.1

$C_{12}H_{15}N_3O_2S$ 265.3

Action and use

Anthelmintic.

DEFINITION

Albendazole contains not less than 98.0 per cent and not more than the equivalent of 102.0 per cent of methyl [5-(propylsulphanyl)-1*H*-benzimidazol-2-yl] carbamate, calculated with reference to the dried substance.

CHARACTERS

A white or faintly yellowish powder, practically insoluble in water, freely soluble in anhydrous formic acid, very slightly soluble in methylene chloride, practically insoluble in ethanol.

IDENTIFICATION

Examine by infrared absorption spectrophotometry *(2.2.24)*, comparing with the spectrum obtained with *albendazole CRS*. Examine the substances prepared as discs.

TESTS

Appearance of solution

Dissolve 0.10 g *albendazole* powder in a mixture of 1 volume of *anhydrous formic acid R* and 9 volumes of *methylene chloride R* and dilute to 10 ml with the same mixture of solvents. The solution is clear *(2.2.1)* and not more intensely coloured than reference solution BY_6 *(2.2.2, Method II).*

Related substances

Examine by liquid chromatography

Test solution Dissolve 25.0 mg of the substance to be examined in 5 ml of *methanol R* containing 1 per cent *V/V* of *sulphuric acid R* and dilute to 50.0 ml with the mobile phase *(300 volumes of 1.67g/l solution of ammonium dihydrogen phosphate R and 700 volumes of methanol R).*

Reference solution (a) Dissolve 10.0 mg of the substance to be examined in 10 ml of *methanol R* containing 1 per cent *V/V* of *sulphuric acid R* and dilute to 100.0 ml with the mobile phase. Dilute 0.5 ml of this solution to 20.0 ml with the mobile phase.

Reference solution (b) Dissolve 50.0 mg of the substance to be examined and 50 mg of *oxybendazole CRS* in 5 ml of *methanol R* containing 1 per cent *V/V* of *sulphuric acid R* and dilute to 100.0 ml with the mobile phase.

The chromatographic procedure may be carried out using:

—a stainless steel column 0.25 m long and 4.6 mm in internal diameter packed with spherical *end-capped octadecylsilyl silica gel for chromatography R* (5 µm) with a pore size of 10 nm and a carbon loading of 19 per cent,

—as the mobile phase at a flow rate of 0.7 ml/min a mixture of 300 volumes of a 1.67 g/l solution of *ammonium dihydrogen phosphate R* and 700 volumes of *methanol R*,

—as detector a spectrophotometer set at 254 nm.

Inject 20 µl of reference solution (a). Adjust the sensitivity of the system so that the height of the principal peak in the chromatogram obtained is at least 50 per cent of the full scale of the recorder. Inject 20 µl of reference solution (b). The test is not valid unless the resolution between the peaks corresponding to albendazole and oxybendazole is at least 3.0.

Inject 20 µl of the test solution. Continue the chromatography for 1.5 times the retention time of albendazole. When the chromatograms are recorded in the prescribed conditions, the approximate relative retention times are: 0.80 for impurity A, 0.43 for impurities B and C, 0.40 for impurity D, 0.47 for impurity E and 0.57 for impurity F. In the chromatogram obtained with the test solution the area of any peak, apart from the principal peak, is not greater than 1.5 times the area of the principal peak in the chromatogram obtained with reference solution (a) (0.75 per cent) and the sum of the areas of any such peaks is not greater than 3 times the area of the principal peak in the chromatogram obtained with reference solution (a) (1.5 per cent). Disregard any peak with an area less than 0.1 times the area of the principal peak in the chromatogram obtained with reference solution (a).

Loss on drying

Not more than 0.5 per cent, determined on 1.000 g by drying in an oven at 100-105 °C for 4 h.

Sulphated ash

Not more than 0.2 per cent, determined on 1.0 g.

ASSAY

In order to avoid overheating during the titration, mix thoroughly throughout and stop the titration immediately after the end-point has been reached.

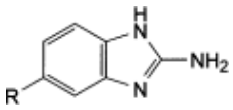
Dissolve 0.250 g in 3 ml of *anhydrous formic acid R* and add 40 ml of *anhydrous acetic acid R*. Titrate with *0.1 M perchloric acid*, determining the end-point potentiometrically *(2.2.20)*.

1 ml of *0.1 M perchloric acid* is equivalent to 26.53 mg of $C_{12}H_{15}N_3O_2S$.

STORAGE

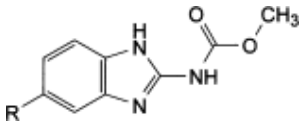
Albendazole should be protected from light.

IMPURITIES



A. R = S-CH_2-CH_2-CH_3: 5-(propylsulphanyl)-1*H*-benzimidazol-2-amine,

D. R = SO_2-CH_2-CH_2-CH_3: 5-(propylsulphonyl)-1*H*-benzimidazol-2-amine,



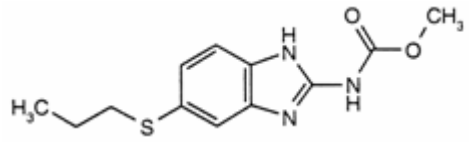
B. R = SO-CH_2-CH_2-CH_3: methyl [5-(propylsulphinyl)-1*H*-benzimidazol-2-yl]carbamate,

C. R = SO_2-CH_2-CH_2-CH_3: methyl [5-(propylsulphonyl)-1*H*-benzimidazol-2-yl]carbamate,

E. R = H: methyl (1*H*-benzimidazol-2-yl)carbamate,

F. R = S-CH_3: methyl [5-(methylsulphanyl)-1*H*-benzimidazol-2-yl]carbamate.

Albendazole (International Pharmacopoiea)



$C_{12}H_{15}N_3O_2S$

Relative molecular mass. 265.3

Chemical name. Methyl 5-(propylthio)-2-benzimidazolecarbamate

Description. A white or almost white powder.

Solubility. Practically insoluble in water; soluble in glacial acetic acid R; slightly soluble in acetone R, very slightly soluble in ethanol (~750 g/l) TS.

Category. Anthelminthic.

Storage. Albendazole should be kept in a well-closed container, protected from light.

Additional information. Melting temperature, about 210°C, with decomposition.

Requirements

Albendazole contains not less than **98.0%** and not more than **101.0%** of $C_{12}H_{15}N_3O_2S$, calculated with reference to the dried substance.

Identity tests

• Either tests A alone or tests B, C, and D may be applied.

A. Carry out the examination as described under 1.7 Spectrophotometry in the infrared region. The infrared absorption spectrum is concordant with the spectrum obtained from albendazole RS or with the *reference spectrum* of albendazole.

B. See the test described below under "Related substances". The principal spot obtained with solution B corresponds in position, appearance, and intensity with that obtained with solution C.

C. Ignite about 0.1 g; fumes are evolved, staining lead acetate paper R black.

D. Add about 0.1 g to 3 ml of sulfuric acid (~100 g/l) TS and warm to dissolve. Add about 1ml of potassium iodobismuthate/acetic acid TS; a reddish brown precipitate is produced.

Sulfated ash: Not more than 1.0 mg/g.

Loss on drying: Dry at 105 °C for 4 hours; it loses not more than 5.0 mg/g.

Related substances: Carry out the test as described under 1.14.1 Thin-layer chromatography, using silica gel R2 as the coating substance and a mixture of 6 volumes of dichloromethane R, 1 volume of ether R, and 1 volume of glacial acetic acid R as the mobile phase. Apply separately to the plate 10 µl of each of 5 solutions in a mixture of 9 volumes of dichloromethane R and 1 volume of anhydrous formic acid R containing (A) 10.0 mg of Albendazole per ml, (B) 1.0 mg of Albendazole per ml, (C) 1.0mg of albendazole RS per ml,

(D) 0.05 mg of albendazole RS per ml, and (E) 0.025 mg of albendazole RS per ml. After removing the plate from the chromatographic chamber, allow it to dry in a current of warm air, and examine the chromatogram in ultraviolet light (254 nm).

Any spot obtained with solution A, other than the principal spot, is not more intense than the principal spot obtained with solution D (0.5%), and only one spot may be more intense than the principal spot obtained with solution E (0.25%).

Assay: Dissolve about 0.25 g, accurately weighed, in 3ml of anhydrous formic acid R, and add 40 ml of glacial acetic acid R1. Then add 0.2 ml of 1-naphtholbenzein/acetic acid TS and titrate with perchloric acid (0.1 mol/l) VS until a green colour is obtained as described under 2.6 Non-aqueous titration, Method A.

Each ml of perchloric acid (0.1 mol/l) VS is equivalent to 26.53mg of $C_{12}H_{15}N_3O_2S$.

Chapter 2

MATERIALS AND METHODS (EXPERIMENTAL)

Materials

2.1.1 **Chemicals and reagents**

Formic acid

Glacial acetic acid

0.1M Perchloric acid VS

Oracet blue indicator

Silica gel

Chloroform

Diethyl ether

Ammonium dihydrogen phosphate

Reagent grade Methanol*(methanol R*)

Potassium dihydrogen orthophosphate

Sulphuric acid

2.1.2 Equipment

Adam-Analytical balance

Cecil CS 2041 UV/Visible Spectrophotometer 2000 series

Fused silica couvettes

Hewlett Packard, HP 3396 Series II integrator

LC-10AT Shimadzu Liquid chromatograph Pump

Applied Biosystems 783 A Programmable absorbance detector

Shimadzu CR 501 Chromatopac

Erweka TA Friabilator

Erweka Disintegrator

Column (C18)

20µl loop size for the injector

0.45 µm PTFE ACRC DISK CR 13 micro filter

Erweka Dissolution Apparatus

Mortar and pestle

Wire nets

Test tubes

Test tube racks

10ml graduated pipette

250ml conical flasks

100ml measuring cylinder

Glass plates

Chromatank

2.1.3 **Drug samples analyzed**

Alben, Zentel, Wormplex, Tanzol, Benzil, Wormzap,Expel, Albendaven,Nesben

METHOD

Sample characterization

2.2.1 Identification of albendazole (infrared spectroscopy)

A small quantity each of the powdered tablet was taken and embedded between the KBr discs for the analysis. For the results, refer to appendix.

2.2.2 Identification of albendazole (samples) using thin layer chromatography

The TLC plates were prepared by layering a silica gel of 0.25mm on a glass plates and activated for 20minutes at 120^{o}C.

The solvent system: a combination of chloroform, glacial acetic acid and ether in the following proportion was used- 60:10:10.

Powdered samples of the tablets including the pure sample were dissolved in glacial acetic acid and spotted on the plates and immersed in the solvent system contained in the chromatank.

The plates were removed when the solvent had moved three-fourths of the length of the plate.

The solvent front was then marked, allowed to evaporate from the plate and examined under short- wavelength U.V light.

2.2.3 Friability test

Ten (10) tablets from a particular brand were released from the blister packed foil and weighed collectively before placing in the friabilator. The tablets were allowed to revolve for 4 minutes approximating to 100 revolutions. The lose tables were removed and reweighed. The method was repeated for the rest of the brands under study. Refer to page 98 of the appendix for tabulated results of the friability test.

2.2.4 Uniformity of weight test

Twenty (20) tablets from a particular brand were released from the blister packed foil and weighed individually and collectively. The differences between the masses of the individual tablets and the mean from the 20 tablets weighed together were calculated. The percentage deviations were also calculated. This method was repeated for the other brands. Refer to appendix for the various tables of weight uniformity test(Tables 1-25).

2.2.5 Disintegration test

Six (6) tablets from each brand was placed in the cylindrical tubes in the disintegration basket. The bottom of the disintegration basket was placed at least 15mm below the surface of the water and the machine was made to operate, whiles the time taken for each tablet to disintegrate was recorded. The same procedure was repeated for the other brands. Refer to pages 100 and 101 of the appendix for tabulated results of the disintegration test.

2.2.6 Dissolution test

900ml of 0.1M HCl solution (as the dissolution medium) was put in the vessel of the dissolution apparatus 2, equilibrated to 37± 0.5 and the thermometer removed. One (1) tablet from each brand was placed in the apparatus taking care to exclude air bubbles and the apparatus immediately operated at 50rpm. Samples were taken at an interval of 15minutes using a 10ml pipette for two hours. However, aliquots withdrawn for analysis were replaced with the dissolution medium.

The aliquots taken were immediately filtered, and their absorbance taken using the U.V spectrophotometer at a wavelength of 292nm where maximum absorbance was recorded. Dilutions were done where necessary.

2.3 HPLC Analysis process

The method used is a combination of the BP and USP methods.

2.3.1 Mobile phase

The mobile phase used was a mixture of 200 volumes of *ammonium dihydrogen phosphate R* and 800 volumes of *methanol R*. The *ammonium dihydrogen phosphate* solution was prepared by dissolving 1.67g in 1000ml of water and adding methanol slowly amidst shaking to avoid overheating.

Sulphuric acid in methanol solution: prepared by adding 1ml of sulphuric acid to 99ml of methanol.

Standard preparation: 100mg of USP albendazole RS, accurately weighed, was transferred to a 50ml volumetric flask. 3ml of **sulphuric acid in methanol solution** was added to 25ml of methanol, and shaken to dissolve. This was diluted with *methanol R* to volume, and mixed. A transfer of 5ml of this stock solution to a second 50ml volumetric flask was done, diluted with methanol to volume, and mixed. A third dilution of 5ml of the resultant solution was made up to 50ml with *methanol R*. A final dilution was made by transferring 5ml of the resultant solution to 50ml with *methanol R*.

Internal standard: 100mg of *mebendazole* pure powder accurately weighed was tranferred into a 50ml volumetric flask. This was dissolved in 3ml of **sulphuric acid in methanol solution** and made up to volume with *methanol R*. 5ml of this stock solution was transferred to a second 50ml volumetric flask and diluted to volume with *methanol R*. A third dilution was made by diluting 5ml of the resultant solution to 50ml with *methanol R.*

Assay Preparation: Twenty (20) tablets of each brand were weighed and powdered. A transfer of an accurately weighed portion of the powder, equivalent to 100mg of albendazole was made to a 50ml volumetric flask. 3ml of **sulphuric acid in methanol was measured** and added with 20ml of *methanol R*, and shaken by mechanical means for about 15minutes. Diluted with *methanol R* to volume, mixed, and filtered, a clear filtrate was obtained (discarding the first

15ml of the filtrate). 5ml of the clear filtrate was transferred to a second 50ml volumetric flask, diluted with *methanol R* to volume, and mixed. 5ml of this solution was transferred to a third 50ml volumetric flask and diluted to volume and mixed. A final dilution was done by transferring 5ml of the solution obtained from the immediate dilution to another 50ml volumetric flask, and made up to volume with *methanol R* and mixing.

Method 1

5ml of the internal standard solution prepared was transferred to 5ml of standard solution or assay preparation in a 50ml volumetric flask and made up to volume with *methanol R.* A series of injections of the resultant solution (six injections) was done into the chromatographic system, equipped with a 254nm detector. The flow rate of 1ml/min was used, and the peak responses recorded. The peak area ratios of the chromatograms obtained from these injections were used for analytical purposes.

Method 2

This procedure is employed when there is no internal standard or where the internal standard selected elutes at the same time as the drug under investigation or interferes with its detection.

By this method, a series of injections of equal proportions of the standard solution was done and the responses recorded at a flow rate of 1ml/min. An average peak area of the repeated injections was done and used for analytical purposes. This method was repeated for the drug samples.

2.3.2 Non –Aqueous Titration

2.3.2.1 Preparation of 0.1M Perchloric Acid

8.5ml of perchloric acid was slowly added to 900ml of glacial acetic acid with continuous and efficient mixing. 30ml of acetic anhydride was slowly added and volume adjusted to one (1) litre with glacial acetic acid and allowed to stand for 24hours before use.

2.3.2.2 Standardization of 0.1M Perchloric acid

0.5g of potassium hydrogen phthalate was accurately weighed into a 100ml conical flask and 25ml of glacial acetic acid added. The solution was warmed to dissolve the salt, cooled and titrated with 0.1M perchloric acid using oracet blue as indicator.

2.3.2.3 Assay of Albendazole tablets (BP)

All the twenty tablets used for the uniformity of weight test were crushed and powdered. An amount of the powder equivalent to 0.250g of albendazole was dissolved in 3ml of anhydrous formic acid and 40ml of anhydrous acetic acid (glacial acetic) was added.

With the aid of a filter paper, the solution was filtered to obtain a clear filtrate.

This was then titrated with 0.1M perchloric acid using oracet blue as indicator.

(1 **ml of *0.1 M perchloric acid* is equivalent to 26.53 mg of $C_{12}H_{15}N_3O_2S$**)

2.4 Worm Paralysis Experiment

This experiment was based on the mode of action of the drug albendazole, which is to paralyse the worm leading to its death. The effective dose (400mg) was used in the investigation. Tablets with the right amount of active ingredient, and exhibit high dissolution rates should paralyse the worms faster.

Two earth worms (*Lumbricus terretis)* of average length 4.5mm, and thickness of about 1.0mm were selected into twelve (12) conical flasks (250ml) each containing 50mls of tyrode solution.

This was done after the worms were washed off sand using ordinary water, and injured worms were left out.

To each of the conical flasks, containing the worms and the tyrode solution, 400mg of each brand of albendazole was crushed, and added. The same was done for the brands of mebendazole - vermox and dewome. These two brands of mebendazole served as positive control for the experiment. Another conical flask containing only the tyrode solution and worms served as the negative control.

To prevent the movement of the active worms from the conical flasks to the outside environment, mesh wire was used to seal the openings at the top. The perforations of the wire mesh allow the flow of air in and out of the conical flasks.

The timing of the movement of the worms within the conical flasks was started soon after the crushed tablets were added and swirled gently to mix. A determination of the movement of the worms was done using blunt edge, such as melting point capillary tubes. By gently touching the worms, movement or otherwise was recorded for the specified time intervals.

Source of worms (*Lumbricus terretis*)

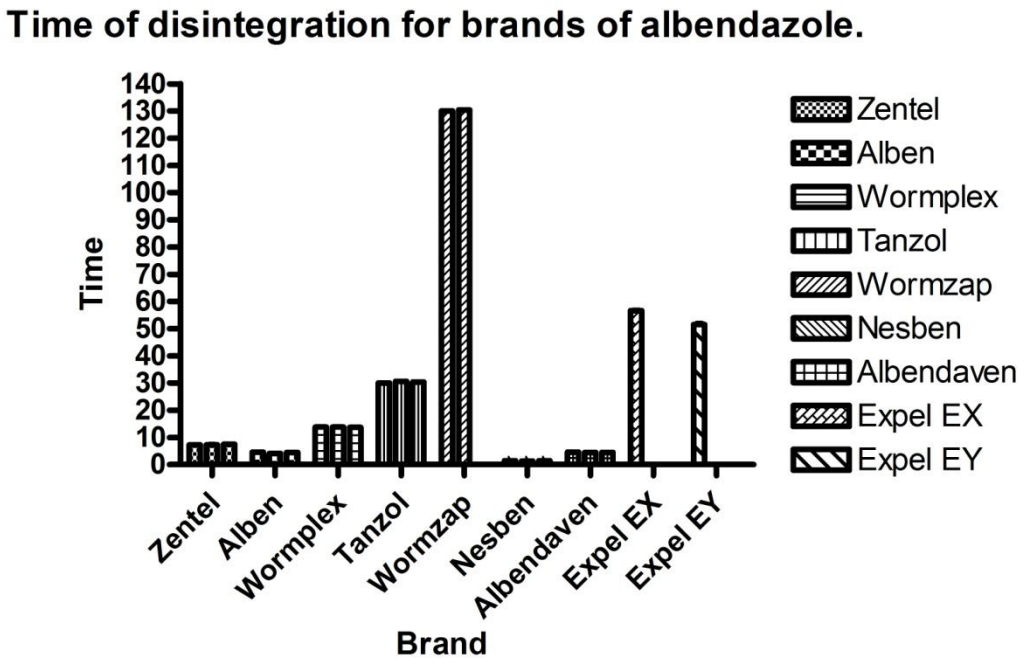
Earth worms thrive in damp, dark rich soil. Hence the worms were dug from a site with such characteristics, which is the soil around the banks of the *Wewe River,* on KNUST campus.

Chapter 3

RESULTS

3.0 Disintegration Time

FIGURE 2.2



Refer to appendix for a tabulation of disintegration time for all batches of the various brands of albendazole

3.1 Non-Aqueous Titration

Calculation of results of non-aqueous titrations

Table 2 Standardization of perchloric acid

W_1 = 0.5008g W_2 = 0.5120g

Expt	1	2
Initial reading/ml	0.00	0.00
Final reading/ml	24.60	24.64
Titre value/ml	24.60	24.64

Average weight of potassium hydrogen phthalate ($C_8H_5O_4K$) used = $\frac{(0.5120 + 0.5008)}{2}$

= 0.5064g

Factor of potassium hydrogen phthalate = Actual weight/ nominal weight

= 0.5064g/0.500g

= **1.0128**

Since mole ratio = 1:1

Average titre = (24.60 + 24.64)/2 = 24.62ml

Factor ($HClO_4$) = factor ($C_8H_5O_4K$) x vol ($C_8H_5O_4K$)/ vol ($HClO_4$)

= (1.0128 x 25ml)/ 24.62ml

= **1.0284**

Hence actual concentration of $HClO_4$ = 1.0284 x 0.1M = **0.1028M**

Table 3 BLANK TITRATION

Expt	1	2
Initial value/ml	0.00	0.20
Final value/ml	0.20	0.40
Titre value/ml	0.20	0.20

Average titre value = (0.20 + 0.20)/2 = 0.20ml

Sample K

Table 4 **W1** = 0.4133g W2 = 0.4139g

Expt	1	2
Initial value	4.00	0.00
Final value	19.20	15.30
Titre value	15.20	15.30

For 1st weight = 0.4133g

Volume of $HClO_4$ consumed = titre value – value from blank titration

= (15.20-0.20) ml

= 15.00ml

Actual volume of $HClO_4$ consumed = 15.00ml x 1.0284 = 15.426ml

From milliequivalence relation :

1ml of 0.1M $HClO_4$ ≡ 0.02653g of albendazole

15.426ml ≡ 15.426ml/1ml x 0.02653g

= 0.40925g

Weight of powder taken = 0.4133g

% Active Ingredient content = 0.40925/ 0.4133 x 100%

= **99.02%**

For 2nd weight = 0.4139g

Volume of $HClO_4$ consumed = (15.30 – 0.20) ml = 15.10ml

Actual volume of $HClO_4$ consumed = 15.10ml x 1.0284 = 15.529ml

From milliequivalence relation

1ml of 0.1M $HClO_4$ ≡ 0.02653g of Albendazole

15.529ml ≡ 15.529ml/1ml x 0.02653g

= 0.41198g

Weight of powder taken = 0.4139g

%Active Ingredient content = 0.41198/ 0.4139g x 100%

= **99.54%**

Average % content of Albendazole in **sample K** = (99.02 + 99.54)/2 = **99.28%**

TITRATION USING PURE ALBENDAZOLE POWDER

Table 5 W1= 0.2505g W2 = 0.2502g

Expt	1	2
Initial value	0.00	0.00
Final value	9.80	9.60
Titre value	9.80	9.60

For 1st weight = 0.2505g

Volume of $HClO_4$ consumed = (9.80 – 0.20) ml = 9.60ml

Actual volume of $HClO_4$ consumed = 9.60ml x 1.0284 = 9.873ml

From milliequivalence relation:

1ml of 0.1M $HClO_4$ ≡ 0.02653g of albendazole

9.873ml ≡ 9.873ml/1ml x 0.02653g

= 0.26192g

% Active ingredient content = 0.26192g/0.2505g x 100%

= **104.56%**

For 2nd weight = 0.2502g

Volume of $HClO_4$ consumed = (9.60-0.20) ml = 9.40ml

Actual volume of $HClO_4$ consumed = 9.40ml x 1.0284 = 9.667ml

From milliequivalence relation:

1ml of 0.1M $HClO_4$ ≡ 0.02653g of albendazole

9.667ml = 9.667ml/1ml x 0.02653g

= 0.25646g

% Active ingredient content = 0.25646g/0.2502g x 100%

= **102.50%**

Average % Active ingredient content = (102.50 + 104.56)/2 = **103.53%**

This method was repeated for all batches of the various brands of albendazole.

Refer to tabulation of results below.

Table 6 % Active ingredient content

Brand/Sample	% content	
	Batch	Titrimetry
Sample K	1	99.28%
	2	99.80%
	3	98.19
Sample F	1	60.97%
	2	70.24%
	3	65.34%
Sample D	1	83.46%
	2	87.22%
	3	89.76%
Sample A	1	83.12%
	2	86.65%
	3	84.80%
Sample B	1	82.89%
	2	84.08%
	3	88.62%
Sample C	1	87.86%
	2	81.43%
	3	85.90%
Sample G	1	57.73%
	2	63.14%
	3	60.71%
Sample E	1	53.28%
	2	51.11%
Sample J(400mg)	1	57.30%
Sample J(200mg)	1	51.07%
SampleH (400mg)	1	56.87%
SampleH (200mg)	1	56.20%

3.2 Dissolution test

U.V analysis

Results of U.V absorbance (whole tablets)

Wavelength of absorbance = 292nm

Table 7

	TIME FOR SAMPLING OF TABLETS IN DISSOLUTION PROCESS(MIN) AND ABSORBANCE(nm)							
DRUG/SAMPLE	15	30	45	60	75	90	105	120
A	*0.761	*0.972	*1.006	*1.098	*1.108	*1.124	*1.181	*1.201
D	*0.292	*0.468	*0.597	*0.724	*0.756	*0.803	*0.878	*0.927
C	*0.674	*0.929	*1.002	*1.081	*1.100	*1.142	*1.165	*1.200
E	*0.028	*0.074	*0.154	*0.208	*0.292	*0.320	*0.375	*0.396
G	*0.396	*0.553	*0.668	*0.778	*0.848	*0.910	*0.936	*0.967
F	*0.764	*0.824	*0.893	*0.996	*1.018	*1.034	*1.042	*1.056
K	0.083	0.152	0.215	0.280	0.334	0.399	0.455	0.481
J	0.111	0.242	0.409	0.642	0.943	1.294	1.500	*0.388
H	0.081	0.153	0.200	0.258	0.317	0.366	0.384	0.424
B	*0.901	*0.998	*1.022	*1.026	*1.116	*1.120	*1.196	*1.214

Key: * - absorbance taken upon using a dilution factor of 10.

Results of U.V absorbance (crushed tablets)

Wavelength of absorbance = 292nm

Table 8

	TIME FOR SAMPLING IN THE DISSOLUTION PROCESS (MIN) AND ABSORBANCE(nm)							
DRUG	15	30	45	60	75	90	105	120
A	*0.853	*1.244	*1.264	*1.372	*1.432	*1.462	*1.476	*1.500
D	*0.703	*0.782	*0.830	*0.943	*1.102	*1.112	*1.158	*1.218
C	*0.741	*0.815	*0.869	*1.121	*1.346	*1.384	*1.382	*1.390
E	*0.107	*0.174	*0.252	*0.282	*0.330	*0.337	*0.354	*0.399
G	*0.647	*0.701	*0.782	*0.855	*0.895	*0.955	*1.008	*1.020
F	*0.751	*0.830	*0.890	*0.905	*0.950	*0.988	*0.997	*1.026
K	1.186	*0.220	*0.268	*0.326	*0.360	*0.412	*0.445	*0.493
J	*0.243	*0.300	*0.383	*0.450	*0.495	*0.521	*0.579	*0.619
H	1.832	*0.282	*0.312	*0.365	*0.393	*0.432	*0.454	*0.439
B	*0.978	*1.372	*1.416	*1.510	*1.516	*1.524	1.548	1.566

Key: * - absorbance taken upon using a dilution factor of 10.

Calculation of concentration ($\%^{w}/_{v}$) for the various absorbance values

A= a*b*c

A: absorbance at 292nm

a: specific absorbance at 292nm (370)

b: path length of the cell, 1cm

c: concentration ($\%^{w}/_{v}$)

Hence c = A/a (since b = 1)

Concentration values at corresponding absorbance value at specified times (whole tablets):

15minutes

For **Sample A**

A = *0.761(* means dilution factor of 10)

a = 370

c = (0.761/370) x 10 = **0.02057%$^{w}/_{v}$**

For Sample **D**

A = *0.292

a = 370

c = (0.292/370) x 10 = **0.00789%$^{w}/_{v}$**

For **Sample C**

A = 0.674

a = 370

c = (0.674/370) x 10 = **0.01821%$^{w}/_{v}$**

This process was followed for the rest of the drugs for the various times of sampling.

Table 9

	TIME FOR SAMPLING IN THE DISSOLUTION PROCESS(MIN) AND CONCENTRATION ($\%^{W}/_{V}$) – WHOLE TABLETS							
DRUG/SAMPLE	15	30	45	60	75	90	105	120
A	0.02057	0.02627	0.027189	0.029676	0.029946	0.030378	0.031919	0.032459
B	0.02435	0.02697	0.02762	0.027729	0.030162	0.03027	0.032324	0.032811
C	0.01821	0.02511	0.02708	0.029216	0.02973	0.030865	0.031486	0.0324324
D	0.00789	0.01265	0.016135	0.019568	0.020432	0.021703	0.023729	0.025054
E	0.0007568	0.002	0.004162	0.005622	0.0078919	0.008649	0.010135	0.010703
F	0.02065	0.02227	0.02414	0.026919	0.0275135	0.027946	0.028162	0.02854
G	0.0107	0.01495	0.018054	0.021027	0.022919	0.024595	0.02529	0.026135
H	0.0002189	0.0004135	0.0005405	0.0006973	0.0008568	0.0009892	0.0009405	0.0011459
J	0.0003	0.000654	0.001105	0.001735	0.002586	0.003497	0.004054	0.0104865
K	0.000224	0.0004108	0.0005811	0.0007568	0.0009027	0.001078	0.012297	0.0013

Table 10 For crushed tablets

	TIME FOR SAMPLING IN THE DISSOLUTION PROCESS(MIN) AND CONCENTRATION ($\%^{w}/_{v}$) – CRUSHED TABLETS							
DRUG/SAMPLE	**15**	**30**	**45**	**60**	**75**	**90**	**105**	**120**
A	**0.023054**	**0.033622**	**0.034162**	**0.037081**	**0.0387027**	**0.0395135**	**0.039892**	**0.040541**
B	**0.026432**	**0.037081**	**0.03827**	**0.04081082**	**0.040973**	**0.0411892**	**0.0418378**	**0.042324**
C	**0.020027**	**0.022027**	**0.0234864**	**0.0302973**	**0.0363784**	**0.0374054**	**0.037351**	**0.0375676**
D	**0.019**	**0.021135**	**0.0224324**	**0.0254865**	**0.029784**	**0.030054**	**0.0312973**	**0.0329189**
E	**0.002892**	**0.004703**	**0.0068108**	**0.0076216**	**0.0089189**	**0.0091081**	**0.0095676**	**0.010784**
F	**0.020297**	**0.0224324**	**0.0240541**	**0.024459**	**0.0256757**	**0.0267027**	**0.026946**	**0.027729**
G	**0.0174865**	**0.018946**	**0.021135**	**0.0231081**	**0.0241892**	**0.0258108**	**0.027243**	**0.027568**
H	**0.004951**	**0.0076216**	**0.0084324**	**0.0098649**	**0.010622**	**0.0116757**	**0.01227**	**0.011865**
J	**0.006568**	**0.008108**	**0.0103514**	**0.0121622**	**0.0133784**	**0.0140811**	**0.0156486**	**0.0167297**
K	**0.0032054**	**0.0059459**	**0.0072432**	**0.0088108**	**0.0097297**	**0.111351**	**0.012027**	**0.013324**

Calculation of percentage (%) of active ingredient released with specific time of sampling:

Dissolution of whole tablets

15minutes

For **Sample A**

$C = 0.02057\%^{w}/_{v} = 0.02057g \equiv 100ml$

Thus in 1000ml:

$0.2057g \equiv 1000ml$

But 0.2057g/1000ml (0.2057g/L) is mass concentration (ρ)

Hence $\rho = 0.2057g/L$

$C = \rho/M$

where C = amount concentration

ρ = mass concentration

M = molar mass (265.3g/mol)

C = (0.2057/265.3)mol/L

= **0.00077535mol/L**

If 400mg pure albendazole tablet (without additives or excipients) was dissolved, the resultant concentration will be as follows:

0.4g ρ ≡ 900ml

X ≡ 1000ml

= 0.4444g/L (ρ)

From the relation:

C = ρ/M

where C = amount concentration

ρ = mass concentration

M = molar mass (265.3g/mol)

C = (0.4444/ 265.3) mol/L

= **0.001675mol/L**

Percentage content released in 15minutes:

% Release = C(tablet)/C(pure sample) x 100%

= 0.00077535/0.001675 x 100%

= **46.289%**

Calculation was similarly done for all other values within the various time intervals. Results of the calculation are tabulated below:

Table 11 PERCENTAGE RELEASED WITH TIME (WHOLE TABLETS)

	% QUANTITY RELEASED WITH TIME(MIN)							
DRUG/SAMPLE	15	30	45	60	75	90	105	120
A	46.29%	59.12%	61.19%	66.78%	67.40%	68.36%	70.48%	73.04%
B	54.80%	60.70%	62.16%	62.40%	67.88%	68.12%	72.74%	73.84%
C	40.99%	56.50%	60.94%	65.75%	66.90%	69.46%	70.86%	72.98%
D	17.76%	28.46%	36.31%	44.03%	45.98%	48.84%	53.40%	56.38%
E	1.70%	4.50%	9.37%	12.63%	17.76%	19.46%	22.81%	24.09%
F	46.47%	50.12%	54.31%	60.58%	61.92%	62.89%	63.37%	64.23%
G	24.15%	33.63%	40.63%	47.32%	51.58%	55.35%	58.46%	58.81%
H	0.49%	0.93%	1.22%	1.57%	1.93%	2.23%	2.34%	2.58%
J	0.68%	0.93%	2.49%	3.91%	5.74%	7.87%	9.12%	23.60%
K	0.51%	0.93%	1.31%	1.70%	2.03%	2.43%	2.767	2.925

Table 12

PERCENTAGE AMOUNT RELEASE WITH TIME (CRUSHED TABLETS)

	% QUANTITY RELEASED WITH TIME (MIN)							
DRUG/SAMPLE	15	30	45	60	75	90	105	120
A	51.88%	75.66%	76.88%	83.45%	87.09%	88.92%	89.77%	91.23%
B	59.482%%	83.45%	86.12%	91.83%	92.20%	92.69%	94.15%	95.24%
C	45.07%	49.57%	52.85%	68.18%	81.86%	84.18%	84.42%	84.54%
D	42.76%	47.56%	50.48%	57.35%	67.02%	67.63%	70.43%	74.08%
E	6.51%	10.58%	15.33%	17.15%	20.07%	20.50%	21.53%	24.27%
F	45.68%	50.48%	54.13%	55.04%	57.78%	60.09%	60.64%	62.40%
G	39.35%	42.64%	47.56%	52.20%	54.43%	58.08%	61.31%	62.04%
H	11.14%	17.15%	18.98%	22.20%	23.90%	26.27%	27.61%	29.74%
J	14.78%	18.26%	23.29%	27.37%	30.11%	31.69%	35.22%	37.68%
K	7.21%	13.38%	16.30%	19.83%	21.90%	25.06%	27.07%	29.98%

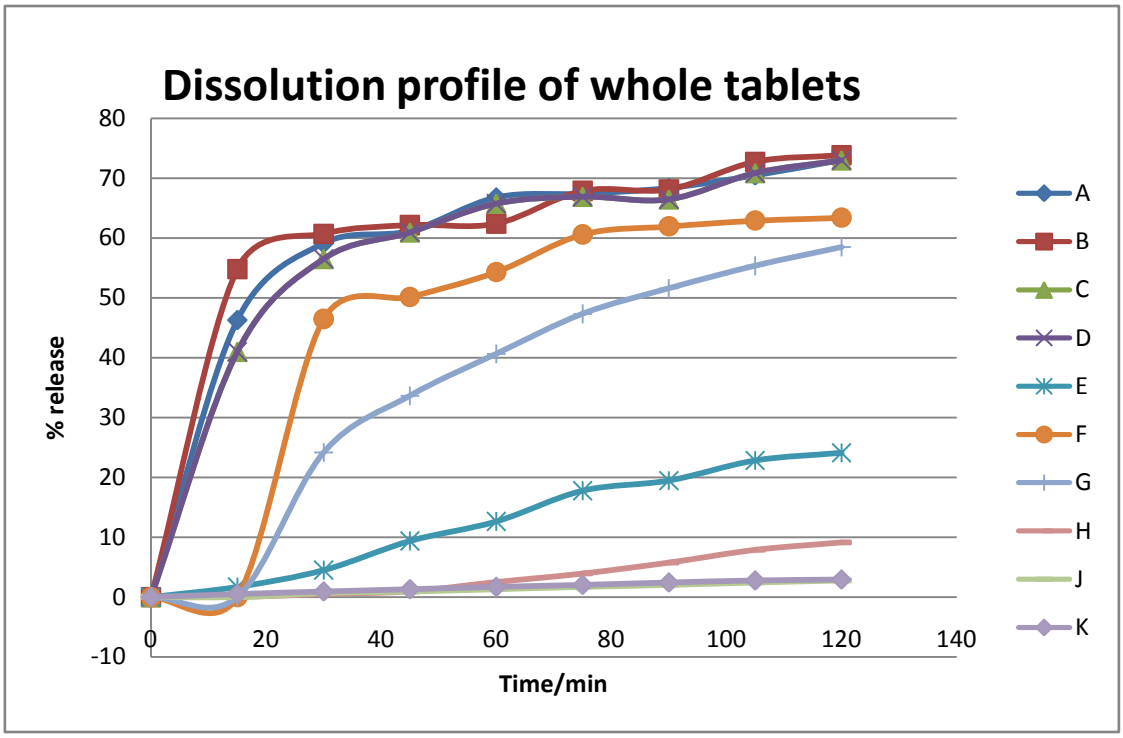

Dissolution profile of whole tablets
% release
Time/min
80
70
60
50
40
30
20
10
0
-10
0
20
40
60
80
100
120
140
A
B
C
D
E
F
G
H
J
K

Figure 2.3

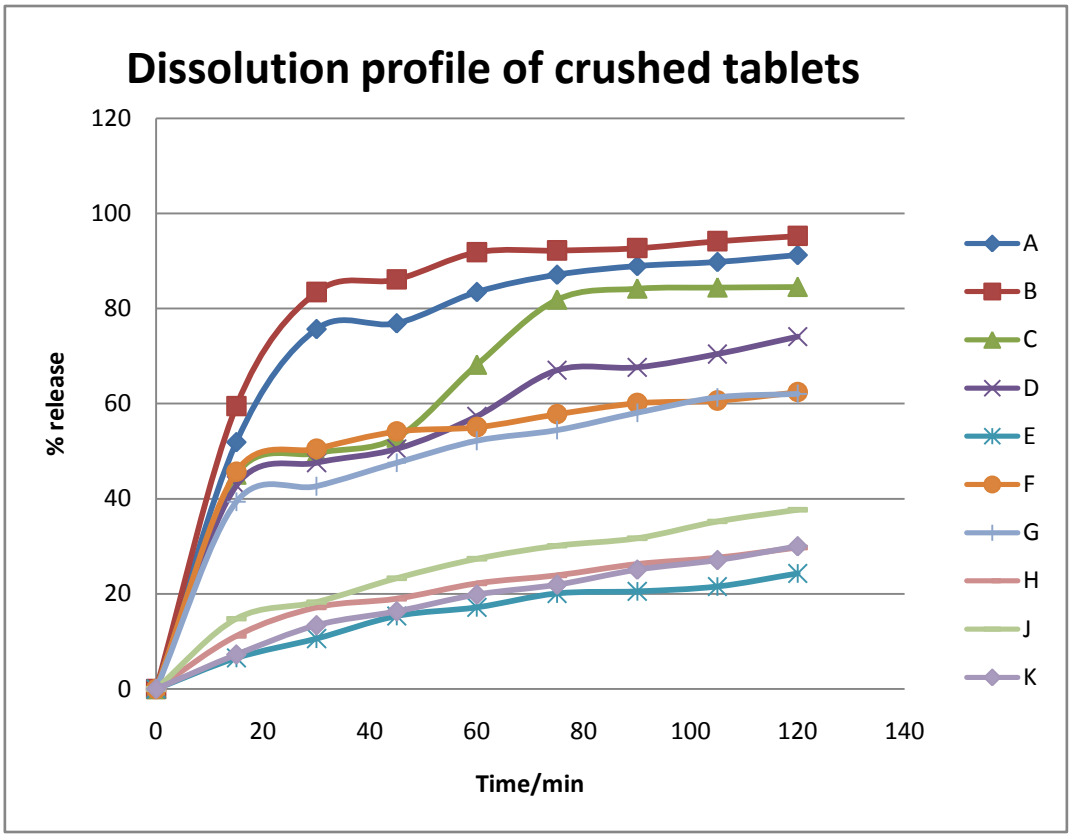

Dissolution profile of crushed tablets
120
100
80
60
40
20
0
% release
0
20
40
60
80
100
120
140
Time/min
A
B
C
D
E
F
G
H
J
K

Figure 2.4

Dissolution of Vermox and Dewome(500mg)

Brand	% Amount release within specified time				
	30min	60min	90min	120min	150min
Vermox	90.00%	102.38%	108.23%	114.07%	131.24%
Dewome(500mg)	88.93%	94.82%	99.63%	108.22%	108.91%

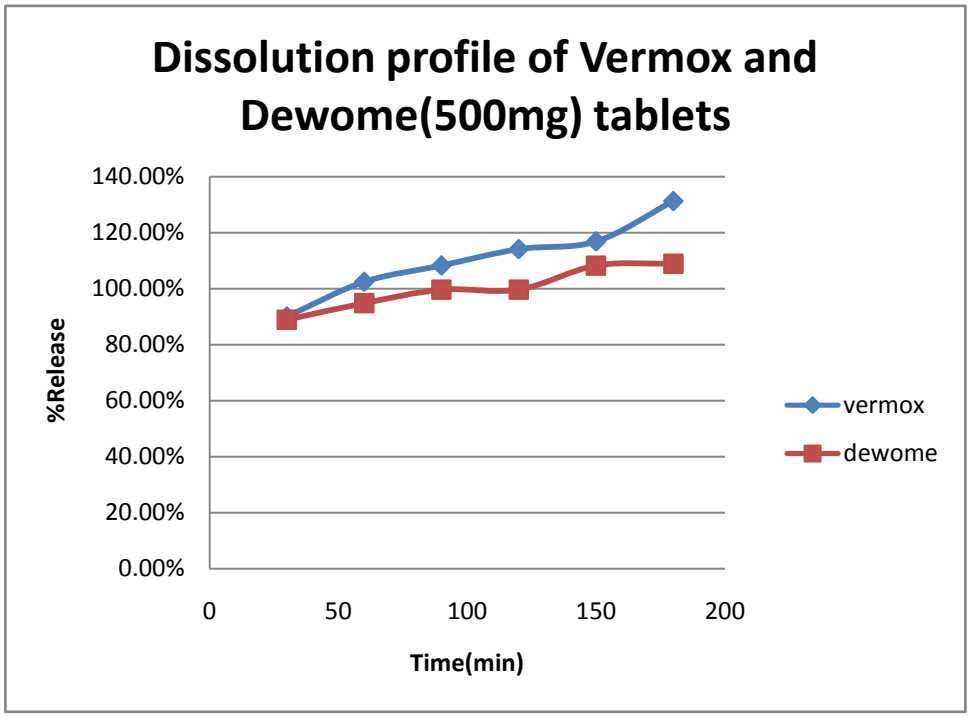


Figure 2.5

SAMPLE OF CHROMATOGRAMS OBTAINED FROM HPLC ANALYSIS OF ALBENDAZOLE AND MEBENDAZOLE

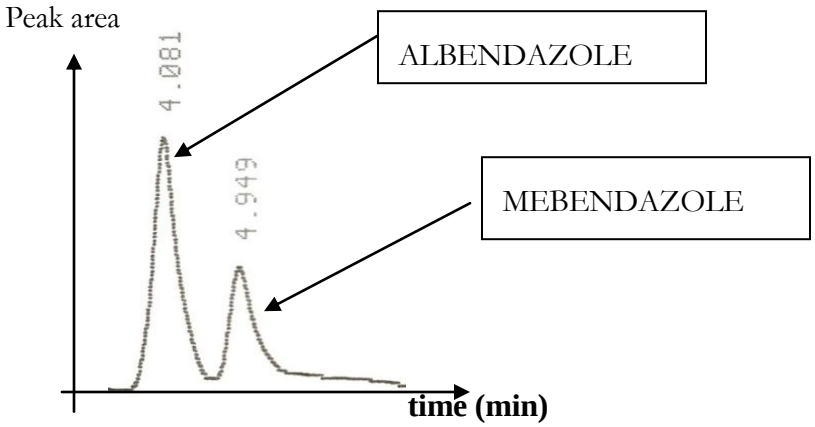


Figure 2.6

CALIBRATION CURVE

USING PEAK AREA

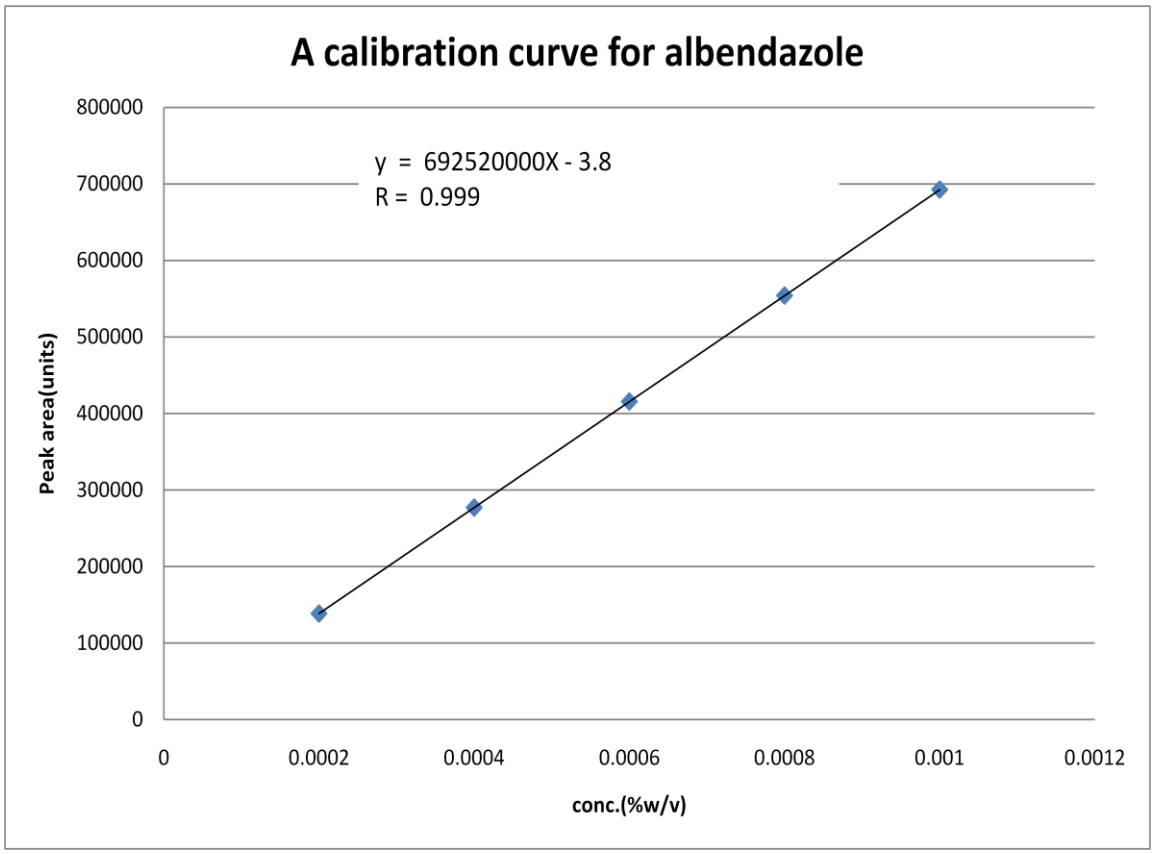


Figure 2.7

USING PEAK AREA RATIO

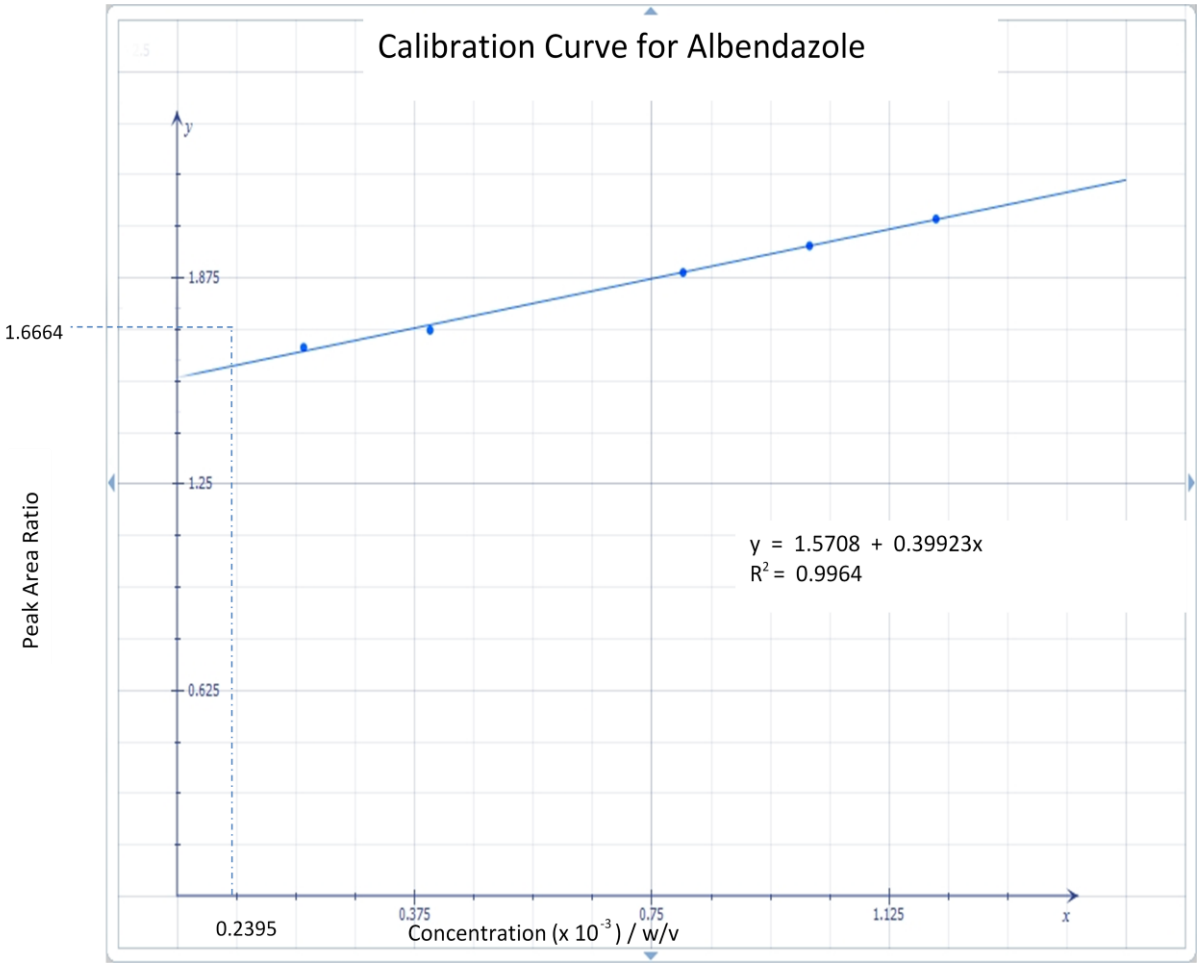


Figure 2.8

3.3 Precision and accuracy determination

3.2.1 Precision Determination (Intra-day)

concentration 0.0002%w/v

Table13

Determination	Peak area (units)
1	138504
2	138501
3	138508
4	138510
5	138503
6	138506
Mean	138505.3
st. deviation	3.326659987
%Relative S.D	0.0024

Table 14 concentration 0.001%w/v

Determination	Peak area (units)
1	692518
2	692522
3	692530
4	692524
5	692516
6	692520
Mean	692521.7
St. deviation(S.D)	4.966554809
%Relative S.D	0.00072

3.2.2 Inter day Precision Determination (using 0.0002%$^{w}/_{v}$)

Table 15

SECOND DAY

NO.	Peak Area
1	138502
2	138508
3	138510
4	138502
5	138514
6	138501
Mean	138506.1667
ST. Deviation	5.30722
%RSD	0.0038317

Table 16

THIRD DAY

NO.	Peak Area
1	138506
2	138512
3	138502
4	138520
5	138501
6	138501
Mean	138507
ST.Deviation	7.64198927
% RSD	0.005517

% Recovery

Table 17

concentration
0.0002%w/v

Determination	% Recovered
1	96.996
2	96.994
3	96.99
4	97
5	96.995
6	96.997
Mean	96.9953
St. deviation(S.D)	0.00332666
%Relative S.D	0.00343

%Recovery

Table 18

concentration
0.001%w/v

Determination	%Recovered
1	96.993
2	96.994
3	96.995
4	96.994
5	96.993
6	96.994
Mean	96.99383
St. deviation	0.000752773
%Relative S.D	0.00776104

3.4 The limit of detection (*LOD*) and limit of quantification (*LOQ)*

LOD = Concentration yielding a signal-to-noise ratio of 2:1

LOQ = Concentration yielding a signal-to-noise ratio of 10:1

3.4.1 LOD

The average base line noise = 1mm

Therefore a concentration yielding a signal to noise ratio of 3:1 should have a peak height of 3x1mm (2mm).

Concentration yielding such a signal- to- noise ratio is 0.00008g/100ml (8ug/ml), therefore LOD = 3 x 8ug/ml = 24ug/ml

OR

LOD= 3 x S.D/slope

= 3 x 3.194/0.39923

= 24.00ug/ml

3.4.2 LOQ

The average base line noise = 1mm

Therefore a concentration yielding a signal to noise ratio of 10:1 should have a peak height of 10x1mm (10mm).

Therefore LOQ = 10 x 8ug/ml = 80ug/ml

OR

LOQ = 10 x S.D/slope

= 10 x 3.194/0.39923

= 80ug/ml

Table 19 Robustness

Condtion	**Variation**	**% Recovered**
flow rate (ml/min)	0.5	99.47
	1	96.99
	1.5	89.26
Wavelength(nm)	254	96.99
	252	96.79
	247	96.98
	245	97.07
Mobile phase (water :methanol content)		
	300:700	100.92
	200:800	99.48

3.5 Worm Experiment

Table 20 Mobility/ paralysis experiment

Drug/Sample	Time of paralysis(min)				
	30	60	90	105	120
Tyrode solution	-	-	-	-	-
A	-	+	++	+ ++	+ +++
B	-	+	+ +	++ +	++ ++
C	-	+	++	+++	+ +++
D	-	-	+	++	+++
G	-	+	++	+++	++++
F	-	+	++	+++	++++
K	-	+	++	+++	++++
E	-	-	+	+ +	+++
H	-	-	+	++	+++
J	-	-	+	++	+++
Dewome	+	++	+++	++++	+++++
Vermox	+	++	+++	++++	+++++

KEY:

(-): no paralysis

(+): paralysis recorded

Volume of tyrode solution used to preserve worms = 50ml

Average length of worms used = 4.5mm

Average size (width) of worms used = 1.0mm

Number of worms used per experiment = 2

Average time of total death for all worms in all brands of albendazole = 3 hours

+ control: vermox and dewome

-control: tyrode solution

3.6 Calculation (HPLC)

Sample calculation for percentage amount recovered

From the equation of graph (using first calibration curve), y = 692520000x-3.8

Y= peak area, x = amount of drug (concentration).

Amount of pure albendazole powder used weighed = 0.1031g

X= y + 3.8 / 692520000

For peak area = 138504,

X= 138504 + 3.8/ 692520000 = 0.0002000g/100ml

Changing this concentration to g/ml: 0.000002000g/ml

Dilution factor = 50000

Hence concentration; 0.000002000g x 50000 = 0.10000274g

% Amount recovered = amount from calculation/ amount weighed x 100

= 0.10000274g/0.1031g x 100

= 96.99%

This calculated is repeated for all values.

However using the second calibration curve, the equation of the line is y = 0.39923x + 1.5708, where y = peak area ratio, x = amount (concentration) the calculation could also be effected.

Calculation for assay of tablets

Average weight of tablet (Sample A) = 0.5489g

Hence 0.2g ≡ 0.5789g *(from average weight)*

0.1g ≡ 0.1/0.2 x 0.5489g

= 0.27445g

Thus 0.27445g of Sample A (200mg) from the batch would contain pure albendazole powder.

However, 0.2779g of the crushed powder was weighed.

Average peak area upon three replicate injections: 385443units

From the equation of graph (using first calibration curve), y = 692520000x-3.8

Y= peak area, x = amount of drug (concentration).

X= y+ 3.8/692520000

X = 385443+3.8/692520000

= 0.0005566g/100ml

Changing 0.0005566g/100ml to g/ml gives: 0.000005566g/ml

X = 0.000005566g/ml

Dilution factor = 50000

Actual amount of drug used= 0.000005566g/ml x 50000 = 0.2783g

Amount of Sample A weighed = 0.2779g

% content = 0.2783g/0.2779g x 100 = **100.14%**

This calculation is repeated for all batches of the various brands of albendazole.

Calculation of percentage active ingredient content (using peak area ratio)

From calibration curve; $y = 1.5708 + 0.39923(10^{-3})\ x$

Where y = peak area ratio

X = amount of drug (concentration)

Using Sample A

y= 1.5819

y-1.5708 = 0.00039923x

1.5819-1.5708 = 0.00039923x

0.0111 = 0.00039923x

27.8235 g/100ml = x

0.2782g/ml = x

Amount of powdered sample A taken = 0.2779g

% Content of sample A = 0.2782g/0.2779g x 100%

= **100.14%**

This calculation is repeated for all brands of albendazole.

Brand/Sample	% content	
	Batch	HPLC
K	1	99.65%
	2	99.18%
	3	99.89%
F	1	88.75%
	2	92.15%
	3	95.67%
D	1	98.75%
	2	98.96%
	3	99.19%
A	1	100.14%
	2	100.47%
	3	99.78%
B	1	99.04%
	2	99.69%
	3	100.02%
C	1	98.48%
	2	99.13%
	3	99.66%
G	1	78.66%
	2	81.29%
	3	79.32%
E	1	61.73%
	2	60.21%
J(400mg)	1	62.02%
J(200mg)	1	76.38%
H(400mg)	1	65.24%
H (200mg)	1	71.49%

Table 21 % Active ingredient content of various brands of albendazole

Chapter 4 DISCUSSION

4.1 Identification of samples

The IR spectra obtained for the samples of albendazole conformed to that of the pure albendazole powder. The presence of the major functional groups was marked in all brands of albendazole.

Using thin layer chromatography, the retention factor (R_f value) for all the brands corresponded to that of the pure albendazole powder. An R_f value of 0.972 was recorded for all brands, using a mobile phase composition of chloroform, glacial acetic acid and diethyl ether in a ratio of 60:10:10. From the identifications tests, the results indicated that the samples were albendazole.

4.2 Friability Test

This test is important in determining the effect of transporting the tablets from the factory to the point of sale or consumption. The effect of rough handling, for instance transporting drugs through bumpy roads, is investigated through the friability test. No tablet is expected to lose more than 1% of its weight, after the test. This was true for all the batches of the various brands of albendazole.

4.3 Weight Uniformity Test

Considering the average weight per tablet for each brand of drug, and for twenty (20) tablets selected at random, no two tablets should deviate by 5% and no single tablet by 10%.

All batches of the various brands of albendazole except sample E passed the uniformity of weight test. **Both batches of sample E failed the uniformity of weight test**.

4.4 Disintegration Test

Complete disintegration is defined as that state in which any residue of the unit, except fragments of insoluble coating or capsule shell, remaining on the screen of the test apparatus is a soft mass having no palpably firm core. There was marked differences in the disintegration time for the various brands of albendazole. These differences basically stem from the differences in the manufacturing procedures (different equipment, different compression weights, etc). Sample F recorded the fastest disintegration time of less than two (2) minutes. Sample B and Sample G recorded an average disintegration time of 4.66minutes. Other disintegration time values recorded for other brands were: sample C, 13.67minutes, sample D, 30minutes, sample A, 7.33minutes, sample H, 56.67minutes and sample J 51.50minutes. The disintegration time recorded for sample E was 2hours 8minutes. The trend remained the same for other batches of the same brands of albendazole.

Though disintegration times for tablets do not bear a direct correlation with dissolution, it is a useful analytical method which should not be ignored. Poor disintegration time values could mean that the manufacturing process needs a review as far as compression pressure, tablet composition, proportion of tablet binder etc are concerned.

4.5 Dissolution Test

The effect of chewing a tablet (albendazole) on dissolution was investigated.

By the standards of the United States Pharmacopoeia (USP), at least 70% of the tablet should be dissolved by 30minutes of the start of the procedure.

The dissolution profile obtained for whole tablets reveals that none of the tablets achieved at least 70% content of the active ingredient dissolved in solution at time 30 minutes. However, sample B recorded the highest dissolution percentage of 60.7%, followed by sample A with the percentage of 59.1%. Sample K which was enteric coated recorded the lowest value. Sample H, though not enteric coated also registered a poor dissolution percentage even after two (2) hours of determination. The values registered for sample K and sample H after two hours, were respectively, 2.9% and 2.5%.

Samples A, B and C tablets however attained a dissolution percentage of more than 70% within two (2) hours of determination. The values were 73.8%, 73.0% and 72.9% respectively.

When the tablets were crushed before dissolution determined, the values recorded indicated geometric increment. At time 30 minutes, the following percentage values were recorded for sample A and B respectively: 83.4% and 75.7%. At time two hours, the following percentages were recorded for samples B, A and C respectively: 95.2%, 91.2% and 84.539%. The percentage dissolution recorded for the other brands after two (2) hours were: sample F 62.4%, sample G 62.0%, sample D 74.1%, sample E 24.3%, sample J 37.7%, sample H 29.7% and sample K, 29.9%.

From the results of the experiment, chewing the tablet of albendazole should increase the dissolution profile. However, there still remains a general problem of dissolution. This is characteristic in the graphs. The formulation of the tablets, and the manufacturing process could be the factors. The crystal structure and size of the granules used for compression could also be contributory factors. Bigger crystals tend to dissolve slowly.

Dissolution characterization of brands of mebendazole, (vermox and dewome), reveals a very good dissolution profile for both. By convention, not less than 75% of mebendazole should be dissolved in solution after 120 minutes. This was clearly met, for each brand recorded a dissolution percentage of 90.0% and 88.9% respectively for vermox and dewome, within thirty (30) minutes of determination. This characteristic proved very useful in the worm paralysis experiment where both brands of mebendazole served as positive control.

4.6 Assay of Product

Titrimetic analysis of the products yielded results of lower percentage content values compared to high performance liquid chromatographic method (HPLC).

According to the standards of the United States pharmacopoeia, upon assay of a product of albendazole, between 90% and 101.0% of the label claim should contain the active ingredient. By this standard, only sample K (all batches) was found to contain active ingredient within the accepted limit, thus, 99.3%, 99.8%, 98.2% via titrimetry.

Using HPLC, the following brands of albendazole and their respective percentage contents were found to be within the acceptable range for all batches used:

Sample K: 99.6%, 99.2%, 99.9%

Sample D: 98.8%, 98.9%, 99.2%

Sample A: 100.1%, 100.5%, 99.8%

Sample B: 99.0%, 99.7%, 100.0%

Sample C: 98.5%, 99.1%, 99.7%

Two batches of sample F recorded percentages within the acceptable range: 92.2%, 95.7%.

The following brands of albendazole however had percentage contents less than the acceptable range of 90%-101.0% for all batches used:

Sample E: 61.7%, 60.2%.

Sample G: 78.7%, 81.3%, 79.3%.

Sample J (400mg): 62.0%.

Sample J (200mg): 76.4%

Sample H (400mg): 65.2%

Sample H (200mg): 71.5%

The standards of the British Pharmacopoeia (BP),states that albendazole contains not less than 98.0% and not more than the equivalent of 102.0% [2]. By these standards the same brands of albendazole passed the test for percentage active ingredient content; samples A, B, C, D, and K with sample F being an exception.

By the standards of the international pharmacopoeia, albendazole should contain not less than **98.0%** and not more than **101.0%** of $C_{12}H_{15}N_3O_2S$, calculated with reference to the dried substance: samples, A, B, C, D and K passed the test via HPLC.

Under titrimetry, and considering the various authorities, only sample K passed the test for the active ingredient content.

4.7 Method Validation

4.7.1 Specificity

Specificity studies were performed by analyzing a standard solution of concentration 0.0002%$^{w}/_{v}$ in the presence and absence of excipients/placebo. The percentage amount recovered upon injection was then determined, for both set of solutions. The average percentage amount recovered for both solutions did not differ significantly; thus 99.992% and 99.995% for solution with excipients and the one without excipients respectively. The following excipients were used: lactose, starch, and saccharin sodium.

4.7.2 Precision

Precision was measured in terms of repeatability of measurement, performed by injecting standard solutions six times and measuring their peak areas. The relative standard deviation (RSD) was found for the determinations as 0.0024 % and 0.00072% for the standard solutions of concentrations 0.0002%^{w}/v and 0.001%$^{w}/_{v}$ respectively. This shows that precision of the method is satisfactory as relative standard deviation is less than 2.0%.

4.7.3 Intermediate Precision

Intermediate precision of the method was determined by analyzing standard solution on different days (first three days) under the same conditions. The values of relative standard deviation obtained are as follows: 0.0024, 0.0038, and 0.0055 for first, second and third days respectively. These values are below 2%; hence intermediate precision of the method is established.

4.7.4 Accuracy

Recovery study was performed to determine the accuracy of the method at two different concentration levels, thus the highest and lowest concentration values used for the calibration curve. Six injections of each concentration were done, and the percentage amount recovered calculated. The average percentage (%) amounts recovered are 96.9953% and 96.9938% respectively for 0.0002%$^{w}/_{v}$ and 0.001%$^{w}/_{v}$. These values are within the acceptance limit.

4.7.5 Robustness

Robustness of the method was determined by analyzing standard solutions at normal operating conditions and also by changing some operating conditions as flow rate, detection wavelength and mobile phase composition. The percentage (%) amount recovered was calculated upon the variation of the operating conditions.

At a flow rate of 0.5ml/min, the recovered amount of 99.47% was recorded, at 1.0ml/min, 96.99% was recorded. At a flow rate of 1.5ml/min, the amount recovered was 89.26%. Flow rates of 1.0ml/min, and 0.5ml/min are the recommended flow rates, since the percentage recovered under these flow rates are within acceptable limits. The retention times for the flow rates were 7.33min, 3.56min and 3.16min for flow rates of 0.5ml/min, 1.0ml/min, and 3.16ml/min respectively.

The change of wavelength of absorbance did not yield a significant difference in the % amount recovered. The wavelengths of 254nm, 252nm, 247nm, and 245nm yielded % recovered amounts of 96.99%, 96.79%, 96.98% and 97.07% respectively.

Variation of the mobile phase composition also yielded results within acceptable limits. The methanol: water composition of 300 volumes of water and 700 volumes of methanol yielded a higher recovered amount of 100.92%. The % recovered amount for 200volumes of water and 800 volumes of methanol is 99.48%.

The chromatograms recorded for the variation in methanol content in the mobile phase indicate significant differences. The chromatograms recorded for 200 volumes of water and 800 volumes of methanol, were almost symmetrical, sharper and well resolved. Those for 300 volume of water and 700 volumes of methanol were broader and unsymmetrical. The mobile phase composition of 200volumes of water and 800 volumes of methanol was chosen.

4.7.6 Linearity

The linearity of the calibration curve is determined by the square of the correlation coefficient, R^2 . The correlation coefficient, R, indicates the degree of linearity between x and y. The R^2 value from the calibration curve was 0.999, which is within the acceptable range of 0.995-0.999, thus linearity of the method is established.

4.8 Worm Paralysis Experiment

This experiment was conducted based on the mode of action of albendazole as an anthelmintic.:

'Albendazole ($C_{12}H_{15}N_3O_2S$) causes degenerative alterations in the tegument and intestinal cells of the worm by binding to the colchicine-sensitive site of tubulin, thus inhibiting its polymerization or assembly into microtubules. The loss of the cytoplasmic microtubules leads to impaired uptake of glucose by the larval and adult stages of the susceptible parasites, and depletes their glycogen stores. Degenerative changes in the endoplasmic reticulum, the mitochondria of the germinal layer, and the subsequent release of lysosomes result in decreased production of adenosine triphosphate (ATP), which is the energy required for the survival of the helminth. Due to diminished energy production, the parasite is immobilized and eventually dies.

Albendazole also has been shown to inhibit the enzyme fumarate reductase, which is helminth-specific. This action may be considered secondary to the effect on the microtubules due to the decreased absorption of glucose. This action occurs in the presence of reduced amounts of nicotinamide-adenine dinucleotide in reduced form (NADH), which is a coenzyme involved in many cellular oxidation-reduction reactions.

Albendazole has larvicidal effects in necatoriasis and ovicidal effects in ascariasis, ancylostomiasis, and trichuriasis.'

The time taken for each brand to achieve this effect was investigated. None of the brands was able to achieve paralysis within the first thirty (30) minutes; paralysis was recorded within one (1) hour. The level of paralysis differed from mild paralysis to total paralysis, (as indicated by +, ++, +++). Brands of mebendazole (Vermox and Dewome) were used as positive controls. For both brands, mild paralysis was recorded within the first thirty (30) minutes. Total death of worms for all brands of albendazole was recorded after three hours of the start of the experiment. The worms in the tyrode solution which served as the negative control were still alive after the three-hour experimentation period.

Several reasons could be assigned to the difference in time of paralysis. The manufacturing process thus, compression pressure, formulation differences and amount of active ingredient present.

Tablets with higher compression pressures would take longer times to disintegrate and dissolve to effect paralysis. Differences in the master formulae of the various brands are worth considering. The differences in formulation means that different amounts of excipients could come into play and different excipients could also be used. Differences in the quantity of binders, diluents, disintegrants etc as well as the crystal structure and size could contribute significantly to the difference in disintegration and dissolution times.

The amount of active ingredient in the various brands of albendazole plays a crucial role in their paralysis effect. Tablets with lower amount of active ingredient would record paralysis after a longer period of time. The converse is true for tablets with higher or the specified amount of active ingredient.

The high dissolution abilities of both brands of mebendazole contributed to the paralysis time recorded. The action of polymorphic forms of mebendazole on the worms was avoided by the use of two brands (i.e. vermox and dewome). Differences in paralysis time of various brands of mebendazole could be investigated using the worm paralysis experiment.

Since polymorphic forms of albendazole appear not to have been reported, reasons other than polymorphism should be considered for difference in paralysis time such as stated above.

Chapter 5

CONCLUSIONS AND RECOMMENDATIONS

4.9 Conclusion

4.9.1 Preliminary tests

The samples used were certified as brands of albendazole.

The various brands of albendazole passed the preliminary tests: uniformity of weight (except sample E) and friability tests.

4.9.2 Disintegration and Dissolution tests

From the results obtained from these tests, it is evident that attention needs to be paid to the manufacturer's information. Chewable tablets should be treated as such. Chewing undoubtedly aids dissolution. Chewing of all brands of albendazole before swallowing is best.

4.9.3 Assay of Products

Titrimetry (non-aqueous titration) is not a sensitive method for the purposes of good and accurate analysis. High performance liquid chromatography (HPLC) is the recommended method of analysis. Its accuracy level is high if a well developed and established method is used.

4.9.4 Method Validation

The method used was found to be specific, precise, accurate and linear.

The method is also robust, flow rates of 0.5ml/min and 1.5ml/min are recommended.

The limit of detection (LOD) from the method and equipment used is 24ug/ml and the limit of quantitation (LOQ) is 80ug/ml.

4.9.5 Worm Paralysis

All brands of albendazole had the ability to paralyse the worms, though the time for this differed from one brand to the other. The ability of the drug to dissolve in solution and the content of the active ingredient in each brand could be responsible for the differences in their time of paralysis. This is evident in the activities of samples A, B and C.

4.9.6 **Recommendations**

The manufacturing process of albendazole needs to be reconsidered. The compression pressures and formulation (level and type of excipients) need particular attention.

Smaller crystals of albendazole powder should be used for tablet compression, since micronization of crystals improves dissolution.

Solubilising agents and disintegrants should be employed or their quantities increased to aid dissolution and disintegration respectively.

Since chewing improves the dissolution, hence the efficacy of the drug, it is recommended that all albendazole tablets be made chewable.

HPLC method not non-aqueous titration is recommended for the assay.[13]

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APPENDIX

Table 1

Tablet	Weight(g)	Deviation	% Deviation
1	0.5682	0.00494	0.494
2	0.5607	-0.00256	-0.256
3	0.5726	0.00934	0.934
4	0.5646	0.00134	0.134
5	0.5772	0.01394	1.394
6	0.5631	-0.00016	-0.016
7	0.5646	0.00134	0.134
8	0.564	0.00074	0.074
9	0.5646	0.00134	0.134
10	0.56	-0.00326	-0.326
11	0.5586	-0.00466	-0.466
12	0.5791	0.01584	1.584
13	0.5554	-0.00786	-0.786
14	0.5657	-0.01756	-1.756
15	0.5684	0.00514	0.514
16	0.5506	-0.01266	-1.266
17	0.5626	-0.00066	-0.066
18	0.5728	0.00954	0.954
19	0.5535	-0.00976	-0.976
20	0.5652	0.00194	0.194
Average weight		0.56326g	
Batch No.			
ALBENDAVEN			

Table 2

Tablet	Weight(g)	Deviation	% Deviation
1	0.5377	-0.0112	-1.12
2	0.5381	-0.0108	-1.08
3	0.5437	-0.0052	-0.52
4	0.5429	-0.006	-0.6
5	0.5381	-0.0108	-1.08
6	0.5492	-0.0003	-0.03
7	0.5442	-0.0047	-0.47
8	0.5494	0.0005	0.05
9	0.5422	-0.0067	-0.67
10	0.5525	0.0036	0.36
11	0.5501	0.0012	0.12
12	0.536	-0.0129	-1.29
13	0.5443	-0.5443	-0.46
14	0.5423	-0.0066	0.66
15	0.5468	-0.0021	-0.21
16	0.5524	0.0035	0.35
17	0.552	0.0031	0.31
18	0.548	-0.0068	-0.68
19	0.548	-0.0009	-0.09
20	0.549	0.0001	0.01

Average weight = 0.5489g

Batch No. 480228

ZENTEL

Table 3

Tablet	Weight	Deviation	% Deviation
1	0.7145	0.000935	0.0935
2	0.7033	-0.010265	-1.0265
3	0.7251	0.011535	1.1535
4	0.714	0.000435	0.0435
5	0.7231	0.009535	0.9535
6	0.7134	-0.000165	-0.0165
7	0.717	0.003435	0.3435
8	0.7086	-0.004965	-0.4965
9	0.7135	-0.000065	-0.0065
10	0.7113	-0.002265	-0.2265
11	0.7238	0.010235	1.0235
12	0.7167	0.003135	0.3135
13	0.7266	0.013035	1.3035
14	0.7084	-0.005165	-0.5165
15	0.7046	-0.008965	-0.8965
16	0.7029	-0.010665	-1.0665
17	0.7129	-0.000665	-0.0665
18	0.7168	0.003235	0.3235
19	0.7058	-0.007765	-0.7765
20	0.7075	-0.006065	-0.6065

Average weight 0.713565g

Batch No

WORMPLEX

Table 4

Tablet	Weight(g)	Deviation	% Deviation
1	0.9603	0.00534	0.534
2	0.914	-0.04096	-4.096
3	0.941	-0.01396	-1.396
4	0.959	0.00404	-0.404
5	0.975	0.02004	-2.004
6	0.936	-0.01896	-1.896
7	0.912	-0.04296	-4.296
8	0.934	-0.02096	-2.096
9	0.977	0.02204	-2.204
10	0.996	0.04104	4.104
11	0.9762	0.02124	2.124
12	0.973	0.01804	1.804
13	0.928	-0.02696	-2.696
14	0.997	0.04204	4.204
15	0.974	0.01904	-1.904
16	0.987	0.03204	3.204
17	0.9511	-0.00386	-0.386
18	0.969	0.01404	1.404
19	0.962	0.00704	0.704
20	0.9616	0.00664	0.664

Average weight 0.95496g

Batch No.

TANZOL

Table5

Tablet	Weight(g)	Deviation	% Deviation
1	1.0483	-0.00048	-0.048
2	1.0371	-0.01168	-1.168
3	1.0397	-0.00908	-0.908
4	1.0451	-0.00368	-0.368
5	1.0489	0.00012	0.012
6	1.048	-0.00078	-0.078
7	1.0531	0.00432	0.432
8	1.0454	-0.00338	-0.338
9	1.0653	0.01652	1.652
10	1.0485	-0.00028	-0.028
11	1.0506	0.00182	0.182
12	1.0424	-0.00638	-0.638
13	1.0439	-0.00488	-0.488
14	1.0495	0.00072	-0.072
15	1.0516	0.00282	0.282
16	1.0491	0.00032	0.032
17	1.0458	-0.00298	-0.298
18	1.0553	0.00702	0.702
19	1.0444	-0.00438	-0.438
20	1.0586	0.00982	0.982
Average weight		1.04878g	
Batch No			
ALBEN			

Table 6

Tablet	Weight(g) X	Deviation	% Deviation
1	0.4546	-0.00107	-0.107
2	0.451	-0.00467	-0.467
3	0.4558	0.00013	0.013
4	0.4687	0.01303	1.303
5	0.4558	0.00013	0.013
6	0.4557	0.00003	0.003
7	0.4613	0.00563	0.563
8	0.4597	0.00403	0.403
9	0.4573	0.00163	0.163
10	0.458	0.00233	0.233
11	0.4348	-0.02087	-2.087
12	0.4552	-0.00047	-0.047
13	0.4582	0.00253	0.253
14	0.4565	0.00083	0.083
15	0.4579	0.00223	0.223
16	0.4585	0.00283	0.283
17	0.4505	-0.00517	-0.517
18	0.4613	0.00563	0.563
19	0.4493	-0.00637	-0.637
20	0.4512	-0.00447	-0.447
Average weight		0.45567g	
Batch No		0106G	
NESBEN			

Table 7

Tablet	Weight	Deviation	%Deviation
1	0.6636	0.00012	0.012
2	0.6661	0.00262	0.262
3	0.6643	0.00082	0.082
4	0.6578	-0.00568	-0.568
5	0.6546	-0.00888	-0.888
6	0.6599	-0.003458	-0.358
7	0.6655	0.00202	0.202
8	0.662	-0.00148	-0.148
9	0.6658	0.00232	0.232
10	0.6546	-0.00888	-0.888
11	0.6521	-0.01138	-1.138
12	0.6536	-0.00988	-0.988
13	0.6611	-0.00238	-0.238
14	0.663	-0.00048	-0.048
15	0.6522	-0.01128	-1.128
16	0.6543	-0.00918	-0.918
17	0.6571	-0.00638	-0.638
18	0.6608	-0.00268	-0.268
19	0.6544	-0.00908	-0.908
20	0.6635	0.00002	0.002

Average weight 0.66348g

Batch No **AL0701**

BENZIL

Table 8

Tablet	Weight	Deviation	% Deviation
1	0.9606	-0.00305	-0.305
2	0.955	-0.00865	-0.865
3	0.9615	-0.00215	-0.215
4	0.9548	-0.00885	-0.885
5	0.9872	0.02355	2.355
6	0.9707	0.00705	0.705
7	0.9556	-0.00805	-0.805
8	0.9513	-0.01235	-1.235
9	0.9636	-0.00005	-0.005
10	0.964	0.00035	0.035
11	0.9646	0.00095	0.095
12	0.9753	0.01165	1.165
13	0.9634	-0.00025	-0.025
14	0.9715	0.00785	0.785
15	0.9701	0.00645	0.645
16	0.9568	-0.00685	-0.685
17	0.9617	-0.00195	-0.195
18	0.9578	-0.00585	-0.585
19	0.9546	-0.00905	-0.905
20	0.9707	0.00705	0.705

Average weight 0.96365g

Batch No BN NO.2

EXPEL 960 EX

Table 9

Tablet	Weight	Deviation	% Deviation
1	0.9623	0.01115	1.115
2	0.9481	-0.00305	-0.305
3	0.9553	0.00415	0.415
4	0.9553	0.00415	0.415
5	0.9393	-0.01185	-1.185
6	0.9289	-0.02225	-2.225
7	0.9529	0.00175	0.175
8	0.9498	0.00865	0.865
9	0.9579	0.00675	0.675
10	0.9549	0.00375	0.375
11	0.9551	0.00395	0.395
12	0.9639	0.01275	1.275
13	0.9101	-0.04105	-4.105
14	0.9569	0.00575	0.575
15	0.9528	0.00165	0.165
16	0.9741	0.02297	2.297
17	0.9407	-0.01045	-1.045
18	0.9645	0.01335	1.335
19	0.9485	-0.00265	-0.265
20	0.9486	-0.00255	-0.255

Average weight 0.95115

Batch No. BN NO.01

EXPEL 960 EY

Table 10

Tablet	Weight	Deviation	% Deviation
1	1.0403	-0.038225	-3.8225
2	1.0519	-0.026625	-2.6625
3	0.9881	-0.090425	-9.0425
4	1.0189	-0.059625	-5.9625
5	0.9878	-0.090725	-9.0725
6	1.0822	0.003675	0.3675
7	1.0509	-0.027625	-2.7625
8	1.0446	-0.033925	-3.3925
9	1.0513	-0.027225	-2.7225
10	1.0489	-0.029625	-2.9625
11	1.038	-0.040525	-4.0525
12	1.0158	-0.062725	-6.2725
13	1.016	-0.062525	-6.2525
14	1.0516	-0.026925	-2.6925
15	1.0242	-0.054325	-5.4325
16	1.0122	-0.066325	-6.6325
17	1.0165	-0.062025	-6.2025
18	1.0396	-0.038925	-3.8925
19	1.0404	-0.038125	-3.8125
20	1.0371	-0.041425	-4.1425

Average weight 1.078525g

Batch No.

WORMZAP

Table 11

Tablet	weight(g)	Deviation	%Deviation
1	0.5621	0.0001	0.01
2	0.5582	0.004	0.4
3	0.5562	0.006	0.6
4	0.5623	0.0001	0.01
5	0.561	0.0012	0.12
6	0.5545	0.0077	0.77
7	0.5562	0.006	0.6
8	0.5568	0.0054	0.54
9	0.5541	0.0081	0.81
10	0.5523	0.0099	0.99
11	0.5611	0.0011	0.11
12	0.5574	0.0048	0.48
13	0.5565	0.0057	0.57
14	0.5588	0.0034	0.34
15	0.5578	0.0044	0.44
16	0.5567	0.0055	0.55
17	0.5632	0.001	0.1
18	0.5571	0.0051	0.51
19	0.5645	0.0023	0.23
20	0.5624	0.0002	0.02

Average weight = 0.5622g

Batch No.

ZENTEL

Table 12

Tablet	weight(g)	Deviation	%Deviation
1	0.5436	0.0016	0.16
2	0.5422	0.003	0.3
3	0.5368	0.0084	0.84
4	0.5433	0.0019	0.19
5	0.5441	0.0011	0.11
6	0.5388	0.0064	0.64
7	0.5511	0.0059	0.59
8	0.5376	0.0076	0.76
9	0.5421	0.0031	0.31
10	0.5371	0.0081	0.81
11	0.5437	0.0015	0.15
12	0.5412	0.004	0.4
13	0.5399	0.0053	0.53
14	0.5427	0.0025	0.25
15	0.5401	0.0051	0.51
16	0.5368	0.0084	0.84
17	0.5382	0.007	0.7
18	0.5384	0.0068	0.68
19	0.543	0.0022	0.22
20	0.5416	0.0036	0.36

Average weight= 0.5452g

Batch No.

ZENTEL

Table 13

Tablet	weight(g)	Deviation	%Deviation
1	0.5711	0.0029	0.29
2	0.572	0.0038	0.38
3	0.5682	0	0
4	0.5678	0.0004	0.04
5	0.5692	0.001	0.1
6	0.5698	0.0016	0.16
7	0.5714	0.0032	0.32
8	0.5687	0.0005	0.05
9	0.5675	0.0007	0.07
10	0.5717	0.0035	0.35
11	0.5709	0.0027	0.27
12	0.5644	0.0038	0.38
13	0.5684	0.0002	0.02
14	0.5599	0.0083	0.83
15	0.5658	0.0024	0.24
16	0.5722	0.004	0.4
17	0.5649	0.0033	0.33
18	0.5676	0.0006	0.06
19	0.5731	0.0049	0.49
20	0.5689	0.0007	0.07

Average weight = 0.5682g

Batch
No.

ALBENDAVEN

Table 14

Tablet	weight(g)	Deviation	%Deviation
1	0.5646	0.0008	0.08
2	0.5771	0.0133	1.33
3	0.5684	0.0046	0.46
4	0.5642	0.0004	0.04
5	0.5714	0.0076	0.76
6	0.5553	0.0085	0.85
7	0.5611	0.0027	0.27
8	0.5589	0.0049	0.49
9	0.5727	0.0089	0.89
10	0.5588	0.005	0.5
11	0.5586	0.0052	0.52
12	0.5536	0.0102	1.02
13	0.5623	0.0015	0.15
14	0.5641	0.0003	0.03
15	0.5641	0.0003	0.03
16	0.5728	0.009	0.9
17	0.561	0.0028	0.28
18	0.5631	0.0007	0.07
19	0.5641	0.0003	0.03
20	0.571	0.0072	0.72

Average weight = 0.5638g

Batch
No.

ALBENDAVEN

Table 15

Tablet	weight(g)	Deviation	%Deviation
1	1.0483	0.0009	0.09
2	1.0422	0.007	0.7
3	1.052	0.0028	0.28
4	1.0461	0.0031	0.31
5	1.0461	0.0031	0.31
6	1.0511	0.0019	0.19
7	1.0451	0.0041	0.41
8	1.0431	0.0061	0.61
9	1.0506	0.0014	0.14
10	1.0501	0.0009	0.09
11	1.0601	0.0109	1.09
12	1.051	0.0018	0.18
13	1.0604	0.0112	1.12
14	1.0452	0.004	0.4
15	1.0444	0.0048	0.48
16	1.0426	0.0066	0.66
17	1.0457	0.0035	0.35
18	1.0441	0.0051	0.51
19	1.0602	0.011	1.1
20	1.0446	0.0046	0.46

Average weight =1.0492

Batch
No.

ALBEN

Table 16

Tablet	weight(g)	Deviation	%Deviation
1	1.0621	0.0039	0.39
2	1.07	0.0118	1.18
3	1.0654	0.0072	0.72
4	1.0624	0.0042	0.42
5	1.0666	0.0084	0.84
6	1.0571	0.0011	0.11
7	1.0641	0.0059	0.59
8	1.0681	0.0099	0.99
9	1.0622	0.004	0.4
10	1.0612	0.003	0.3
11	1.0651	0.0069	0.69
12	1.0596	0.0014	0.14
13	1.0671	0.0089	0.89
14	1.0628	0.0046	0.46
15	1.0656	0.0074	0.76
16	1.0621	0.0039	0.39
17	1.0646	0.0064	0.64
18	1.0644	0.0062	0.62
19	1.0677	0.0095	0.95
20	1.0597	0.0015	0.15

Average weight = 1.0582

Batch
No.

ALBEN

Table 17

Tablet	weight(g)	Deviation	%Deviation
1	0.7401	0.0144	1.44
2	0.7218	0.0039	0.39
3	0.7242	0.0015	0.15
4	0.7144	0.0113	1.13
5	0.7231	0.0026	0.26
6	0.7327	0.007	0.7
7	0.7235	0.0022	0.22
8	0.7341	0.0084	0.84
9	0.7371	0.0114	1.14
10	0.7255	0.0002	0.02
11	0.7268	0.0011	0.11
12	0.7199	0.0058	0.58
13	0.724	0.0017	0.17
14	0.7345	0.0088	0.88
15	0.7244	0.0013	0.13
16	0.7263	0.0006	0.06
17	0.7317	0.006	0.6
18	0.7419	0.0162	1.62
19	0.7365	0.0108	1.08
20	0.7268	0.0011	0.11

Average weight = 0.7257g

Batch No.

WORMPLEX

Table 18

Tablet	weight(g)	Deviation	%Deviation
1	0.7124	0.0019	0.19
2	0.7211	0.0068	0.68
3	0.7127	0.0016	0.16
4	0.7085	0.0058	0.58
5	0.7108	0.0035	0.35
6	0.7232	0.0089	0.89
7	0.7218	0.0075	0.75
8	0.7022	0.0121	1.21
9	0.7147	0.0004	0.04
10	0.7122	0.0021	0.21
11	0.7156	0.0013	0.13
12	0.7076	0.0067	0.67
13	0.7144	0.0001	0.01
14	0.7132	0.0011	0.11
15	0.7201	0.0058	0.58
16	0.7166	0.0023	0.23
17	0.7212	0.0069	0.69
18	0.7125	0.0018	0.18
19	0.7154	0.0011	0.11
20	0.7129	0.0014	0.14

Average weight = 0.7143g

Batch No.

WORMPLEX

Table 19

Tablet	weight(g)	Deviation	%Deviation
1	0.9643	0.0028	0.28
2	0.9626	0.0045	0.45
3	0.9712	0.0041	0.41
4	0.9635	0.0036	0.36
5	0.9688	0.0017	0.17
6	0.9622	0.0049	0.49
7	0.9661	0.001	0.1
8	0.9686	0.0015	0.15
9	0.9723	0.0052	0.52
10	0.9708	0.0037	0.37
11	0.9701	0.003	0.3
12	0.9611	0.006	0.6
13	0.9633	0.0038	0.38
14	0.9677	0.0006	0.06
15	0.9687	0.0016	0.16
16	0.9744	0.0073	0.73
17	0.9646	0.0025	0.25
18	0.9667	0.0004	0.04
19	0.9737	0.0066	0.66
20	0.9679	0.0008	0.08

Average weight = 0.9671g

Batch No.

TANZOL

Table 20

Tablet	weight(g)	Deviation	%Deviation
1	0.9612	0.0099	0.99
2	0.9843	0.0132	1.32
3	0.9646	0.0065	0.65
4	0.9765	0.0054	0.54
5	0.9764	0.0053	0.53
6	0.9678	0.0033	0.33
7	0.9663	0.0048	0.48
8	0.9722	0.0011	0.11
9	0.964	0.0071	0.71
10	0.9695	0.0016	0.16
11	0.9623	0.0088	0.88
12	0.9745	0.0034	0.34
13	0.9741	0.003	0.3
14	0.9677	0.0034	0.34
15	0.9661	0.005	0.5
16	0.9736	0.0025	0.25
17	0.9643	0.0068	0.68
18	0.9714	0.0004	0.04
19	0.9734	0.0023	0.23
20	0.9631	0.008	0.8

Average weight = 0.9711

Batch No.

TANZOL

Table 21

Tablet	weight(g)	Deviation	%Deviation
1	0.4614	0.0021	0.21
2	0.4587	0.0048	0.48
3	0.4349	0.0286	2.86
4	0.4554	0.008	0.8
5	0.4643	0.0008	0.08
6	0.4545	0.009	0.9
7	0.4376	0.0259	2.59
8	0.4566	0.0069	0.69
9	0.4613	0.0022	0.22
10	0.4622	0.0013	0.13
11	0.4561	0.0074	0.74
12	0.4532	0.0103	1.03
13	0.4619	0.0016	0.16
14	0.4548	0.0087	0.87
15	0.4701	0.0066	0.66
16	0.4565	0.007	0.7
17	0.4483	0.0197	1.97
18	0.4622	0.0013	0.13
19	0.4641	0.0006	0.06
20	0.4488	0.0147	1.47

Average weight = 0.4635

Batch No.

NESBEN

Table 22

Tablet	weight(g)	Deviation	%Deviation
1	0.4581	0.005	0.5
2	0.4587	0.0056	0.56
3	0.4566	0.0035	0.35
4	0.4611	0.008	0.8
5	0.4534	0.0003	0.03
6	0.4524	0.0007	0.07
7	0.4581	0.005	0.5
8	0.4468	0.0063	0.63
9	0.4465	0.0066	0.66
10	0.4395	0.0136	1.36
11	0.4377	0.0154	1.54
12	0.4363	0.0168	1.68
13	0.4388	0.0143	1.43
14	0.4443	0.0088	0.88
15	0.4522	0.0009	0.09
16	0.4387	0.0144	1.44
17	0.4441	0.009	0.9
18	0.4519	0.0012	0.12
19	0.4452	0.0079	0.79
20	0.4623	0.0092	0.92

Average weight = 0.4531g

Batch No.

NESBEN

the use of chrom[14]

use of conditions[15]

wonderful idea[16]

good[17]

Table 17

Table 19

Table 23

Tablet	weight(g)	Deviation	%Deviation
1	0.6634	0.0005	0.05
2	0.6658	0.0029	0.29
3	0.6615	0.0014	0.14
4	0.6547	0.0082	0.82
5	0.6598	0.0031	0.31
6	0.6653	0.0024	0.24
7	0.6527	0.0102	1.02
8	0.6588	0.0041	0.41
9	0.6631	0.0002	0.02
10	0.6609	0.002	0.2
11	0.6575	0.0054	0.54
12	0.6711	0.0082	0.82
13	0.6539	0.009	0.9
14	0.6622	0.0007	0.07
15	0.6645	0.0016	0.16
16	0.6566	0.0063	0.63
17	0.6627	0.0002	0.02
18	0.6717	0.0088	0.88
19	0.6643	0.0014	0.14
20	0.6633	0.0004	0.044

Average weight = 0.6629g

Batch No.

BENZIL

Table 24

Tablet	weight(g)	Deviation	%Deviation
1	0.6608	0.0033	0.33
2	0.663	0.0011	0.11
3	0.6571	0.007	0.7
4	0.6635	0.0006	0.06
5	0.6609	0.0032	0.32
6	0.6643	0.0002	0.02
7	0.6578	0.0063	0.63
8	0.6722	0.0081	0.81
9	0.659	0.0051	0.51
10	0.6627	0.0014	0.14
11	0.6614	0.0027	0.27
12	0.6589	0.0052	0.52
13	0.6637	0.0004	0.04
14	0.6574	0.0067	0.67
15	0.6621	0.002	0.2
16	0.6569	0.0072	0.72
17	0.6666	0.0025	0.25
18	0.6721	0.008	0.8
19	0.6576	0.0065	0.65
20	0.6655	0.0014	0.14

Average weight = 0.6641g

Batch No.

BENZIL

Table 25

Tablet	weight(g)	Deviation	%Deviation
1	1.0203	0.0618	6.18
2	1.0505	0.0316	3.16
3	1.0152	0.0669	6.69
4	1.0442	0.0379	3.79
5	1.0422	0.0399	3.99
6	1.0187	0.0634	6.34
7	1.0541	0.028	2.8
8	1.0365	0.0456	4.56
9	1.0882	0.006	0.6
10	1.0518	0.0303	3.03
11	0.9984	0.0837	8.37
12	1.0231	0.059	5.9
13	0.9992	0.0829	8.29
14	1.0651	0.017	1.7
15	1.0211	0.061	6.1
16	1.0227	0.0594	5.94
17	1.0142	0.0679	6.79
18	1.0155	0.0666	6.66
19	1.0121	0.07	7
20	1.0575	0.0246	2.46

Average weight = 1.0821g

Batch No.

WORMZAP

PRECISION

Table26
concentration0.0002%w/v

Dilution factor= 50000

Determination	Peak area (units)
1	138504
2	138501
3	138508
4	138510
5	138503
6	138506
Mean	138505.3
st. deviation	3.326659987
Relative S.D	0.0024

Table 27 concentration 0.001%w/v

Dilution factor = 10000

Determination	Peak area (units)
1	692518
2	692522
3	692530
4	692524
5	692516
6	692520
Mean	692521.7
St. deviation(S.D)	4.966554809
Relative S.D	0.00072

Table 28

% Recovery

concentration
0.0002%w/v

Determination	% Recovered
1	96.996
2	96.994
3	96.99
4	97
5	96.995
6	96.997
Mean	96.9953
St. deviation(S.D)	0.00332666
Relative S.D	0.00343

Table 29

concentration
0.001%w/v

Determination	%Recovered
1	96.993
2	96.994
3	96.995
4	96.994
5	96.993
6	96.994
Mean	96.99383
St. deviation	0.000752773
Relative S.D	0.00776104

Table 29

Table 30 Table for calibration curve

Concentration(%w/v)	Peak area (units)
0.0002	138504
0.0004	277002
0.0006	415503
0.0008	554014
0.001	692518

Table 31

SECOND DAY(Precision)

NO.	Peak Area
1	138502
2	138508
3	138510
4	138502
5	138514
6	138501
Mean	138506.1667
ST. Deviation	5.30722
%RSD	0.0038317

Table 32

THIRD DAY

NO.	Peak Area
1	138506
2	138512
3	138502
4	138520
5	138501
6	138501
Mean	138507
ST.Deviation	7.64198927
% RSD	0.005517

Table 33 Flow rate: 1.5ml/min(0.0002%w/v)

Determination	% Recovered
1	89.263
2	89.268
3	89.262
4	89.271
5	89.262
6	89.258
Average % recovered	89.264

Table 34 Flow rate :

0.5ml/min(0.0002%w/v)

Determination	% Recovered
1	99.475
2	99.478
3	99.474
4	99.473
5	99.465
6	99.472
Average % recovered	99.473

Table 35(wavelength variation)

Wavelength(nm)	% Recovered
254	96.99
252	96.79
247	96.98
245	97.07
St. Deviation	0.118708326
%RSD	0.1224

Table 36

Flow rate: 1.5ml/min(0.0002%w/v)

Determination	Peak area
1	127462
2	127469
3	127461
4	127473
5	127461
6	127455

Table37 Wavelength(robustness)

Wavelength (nm)	Peak area(units)
254	138504
252	138216
247	138489
245	138613

Table 38

Determination	% Recovered
1	100.92
2	100.93
3	100.9
4	100.93
Average	100.92

Table 40 Mobile phase variation

Mobile phase composition	% Recovered
300 vol water: 700vol methanol	100.92
200vol water: 700vol methanol	99.48

Table 39 calculation

(Mobile phase)-robustness

Determination	Peak Area
1	144113
2	144126
3	144091
4	144122

Table 41 Friability test

Brand	Batch	Weight(g)			
		Before test	After test	Wt. Loss(g)	%Wt Loss
Zentel(200mg)	1	5.451	5.448	0.003	0.06%
	2	5.542	5.538	0.004	0.072
	3	5.482	5.468	0.014	0.026
Alben(400mg)	1	10.5111	10.5108	0.0003	0.0028
	2	10.5321	10.5301	0.002	0.0189
	3	10.5261	10.524	0.0021	0.0199
Wormplex (400mg)	1	7.143	7.1426	0.0004	0.0056
	2	7.1836	7.1785	0.0051	0.0709
	3	7.2114	7.2101	0.0013	0.018
Tanzol (400mg)	1	9.5541	9.5522	0.0019	0.0198
	2	9.5633	9.561	0.0023	0.024
	3	9.5377	9.5323	0.0054	0.057
Expel EX	1	9.6421	9.6418	0.0003	0.0031
Expel EY	1	9.5211	9.5205	0.0006	0.0063
Albendaven(200mg)	1	5.632	5.6297	0.0023	0.0408
	2	5.5828	5.5766	0.0062	0.111
	3	5.6412	5.6319	0.0093	0.1649
Nesben (200mg)	1	4.5543	4.5538	0.0005	0.0109
	2	4.5622	4.5603	0.0019	0.0416
	3	4.5581	4.5523	0.0058	0.1272
Wormzap (400mg)	1	10.7218	10.7197	0.0021	0.0196
	2	10.7432	10.7382	0.005	0.0465

Table 42 %Active ingredient Content

Brand	% Active ingredient content		
	Batch	Titrimetry	HPLC
Benzil(400mg)	1	99.28%	99.65%
	2	99.80%	99.18%
	3	98.19	99.89%
Nesben(200mg)	1	60.97%	88.75%
	2	70.24%	92.15%
	3	65.34%	95.67%
Tanzol(400mg)	1	83.46%	98.75%
	2	87.22%	98.96%
	3	89.76%	99.19%
Zentel (200mg)	1	83.12%	100.14%
	2	86.65%	100.47%
	3	84.80%	99.78%
Alben(400mg)	1	82.89%	99.04%
	2	84.08%	99.69%
	3	88.62%	100.02%
Wormplex (400mg)	1	87.86%	98.48%
	2	81.43%	99.13%
	3	85.90%	99.66%
Albendaven(200mg)	1	57.73%	78.66%
	2	63.14%	81.29%
	3	60.71%	79.32%
Wormzap(400mg)	1	53.28%	61.73%
	2	51.11%	60.21%
Expel EY(400mg)	1	57.30%	62.02%
Expel EY(200mg)	1	51.07%	76.38%
Expel EX (400mg)	1	56.87%	65.24%
Expel EX (200mg)	1	56.20%	71.49%

Disintegration Time (First Batch)

Tablet	Disintegration Time (min)						Average Disintegration time(min)	Batch
Zentel	7	8	7	7	7	8	7.33	1
Alben	4	5	6	4	5	4	4.33	1
Wormplex	14	13	14	15	13	14	13.67	1
Tanzol	30	30	30	31	30	29	30	1
Wormzap	130	129	130	131	130	130	130	1
Expel Ex	55	57	58	56	58	56	56.67	1
Expel Ey	50	51	50	55	52	51	51.5	1
Albendaven	5	4	6	4	5	4	4.33	1
Nesben	1.4	1.42	1.4	1.44	1.42	1.4	1.41	1

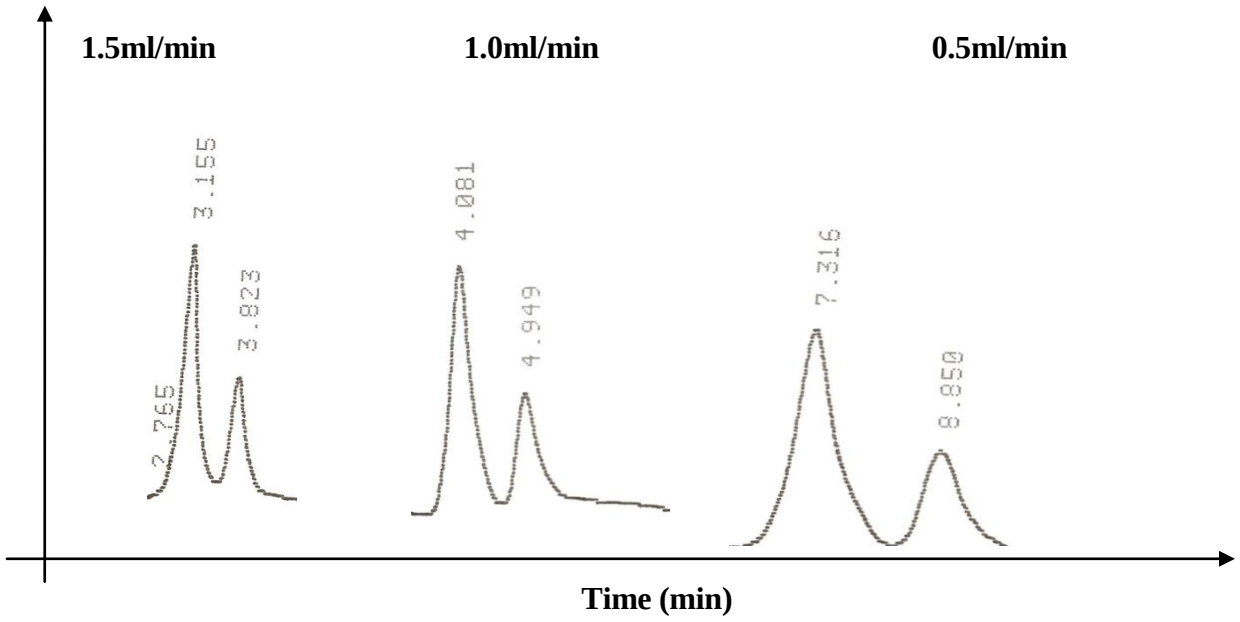
Table 42 Disintegration time (second batch)

Tablet	Disintegration Time (min)						Average Disintegration time(min)	Batch
Zentel	7	8	8	7	6	7	7.16	2
Alben	4	4	4	4	5	4	4.16	2
Wormplex	14	15	14	14	13	14	14	2
Tanzol	30	30	32	31	30	31	30.6	2
Wormzap	130	132	130	130	130	130	130.33	2
Albendaven	5	4	5	4	5	4	4.5	2
Nesben	1.4	1.42	1.36	1.44	1.4	1.4	1.4	2

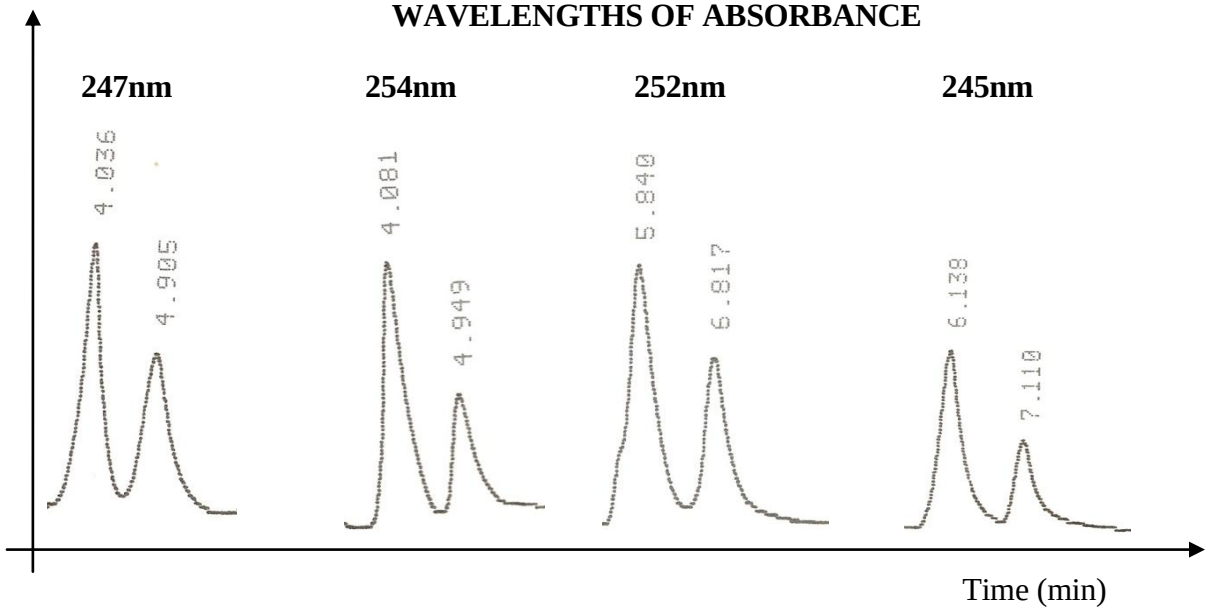
Table 43 Disintegration time (third batch)

Tablet	Disintegration Time (min)						AverageDisintegration time(min)	Batch
Zentel	7	8	8	8	7	7	7.5	3
Alben	4	5	4	5	5	4	4.5	3
Wormplex	14	15	14	14	13	14	14	3
Tanzol	30	31	30	30	30	31	30.33	3
Albendaven	5	4	5	4	5	4	4.5	3
Nesben	1.4	1.42	1.4	1.44	1.38	1.4	1.41	3

FLOW RATES

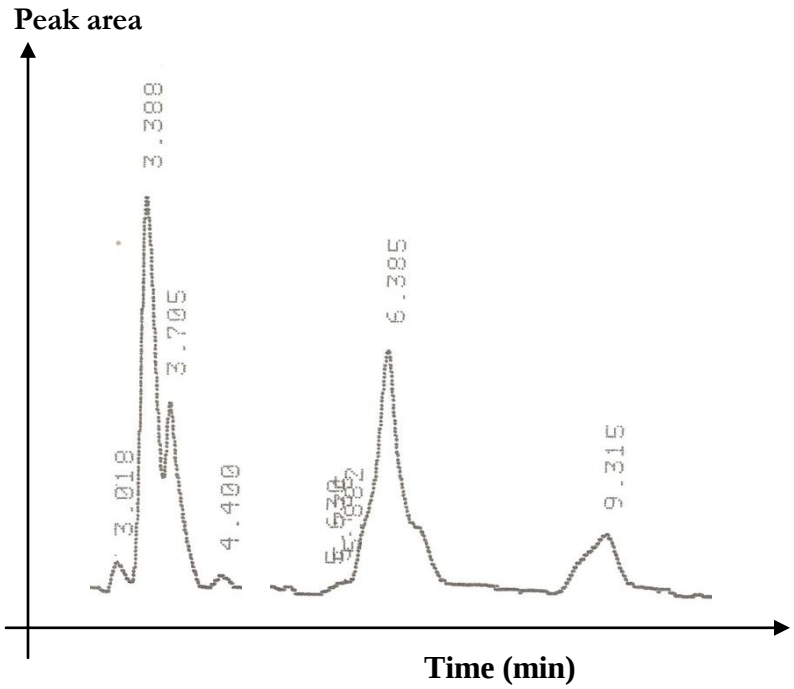


WAVELENGTHS OF ABSORBANCE



MOBILE PHASE COMPOSITION

100vol of H_20: 900 vol of methanol 300vol of H_20: 700vol of methanol



SAMPLES USED

Zentel(200mg) : A

A1: Batch 1: 390272

A2: Batch 2: 480228

A3: Batch 3:380525

Prescribed mode of administration: could be chewed or swallowed whole.

Manufacturer: SmithKline Beecham (SB) Laboratories Pharmaceutiques

Alben (400mg): B

B1: Batch 1: 480091

B2: Batch 2:480231

B3: Batch 3:003*

Prescribed mode of administration: could be chewed or swallowed whole.

Manufacturer: SmithKline Beecham (SB) Pharmaceuticals, Brentford, England.

Wormplex(400mg): C

C1: Batch 1: WPFH0016

C2: Batch 2:WPTK8004

C3: Batch 3:WPTK8002

Prescribed mode of administration: Not stated, if to be chewed or swallowed whole.

Manufacturer: Micro Labs Limited, 92, SIPCOT, HOSUR-635126, India

Tanzol(400mg): D

D1: Batch 1: 003(code MH/DRUGS/KD-818A)

D2: Batch 2: 001 (code MH/DRUGS/DD-2103-A)

D3: Batch 3: SG004

Prescribed mode of administration: To be chewed before swallowing

Manufacturer: Shalina Laboratories PVT.Ltd, 96, Maker Chambers VI, Narmian Point, Mumbai-India.

Wormzap(400mg): E

E1: Batch 1:AL090604

E2: Batch 2: AL090201

E3: Batch 3:AL090503

Prescribed mode of administration: Could be chewed or swallowed whole.

Manufacturer:GR Industries Limited, Plot No.74, South Industrial Area, Fadama Road, Accra, Ghana.

Nesben(200mg): F

F1: Batch 1: 0106G

F2: Batch 2: 002*

F3: Batch 3: 003*

Prescribed mode of administration: Not stated if tablet is chewed or swallowed whole.

Manufacturer: Ernest Chemists Ltd, P.O.Box 3345 Accra, Ghana.

Albendaven(200mg): G

G1: Batch 1:ALB2010801

G2: Batch 2: 002*

G3: Batch 3: 003*

Prescribed mode of administration: To be chewed before swallowing.

Manufacturer: Wexford Laboratories PVT. LTD, India.

Expel Ex (200mg, 400mg): H

H1: BN 002

Prescribed mode of administration: Not stated

Manufacturer: Letap Pharmaceuticals, Ghana

Expel 960 Ey (200mg, 400mg): J

J: BN 001

Prescribed mode of administration: Not stated

Manufacturer: Letap Pharmaceuticals, Ghana

Benzil (400mg): K

J1: Batch 1: 001*

J2: Batch 2: AL0701

Prescribed mode of administration: To be chewed before swallowing.

Manufacturer: Mission Pharmaceuticals Limited, 54-B, Drug House, Procter Road, Mumbai 400 007, INDIA.

Table 6

Table5

Tablet	Weight(g)	Deviation	% Deviation
1	1.0483	-0.00048	-0.048
2	1.0371	-0.01168	-1.168
3	1.0397	-0.00908	-0.908
4	1.0451	-0.00368	-0.368
5	1.0489	0.00012	0.012
6	1.048	-0.00078	-0.078
7	1.0531	0.00432	0.432
8	1.0454	-0.00338	-0.338
9	1.0653	0.01652	1.652
10	1.0485	-0.00028	-0.028
11	1.0506	0.00182	0.182
12	1.0424	-0.00638	-0.638
13	1.0439	-0.00488	-0.488
14	1.0495	0.00072	-0.072
15	1.0516	0.00282	0.282
16	1.0491	0.00032	0.032

17	1.0458	-0.00298	-0.298
18	1.0553	0.00702	0.702
19	1.0444	-0.00438	-0.438
20	1.0586	0.00982	0.982

Average weight 1.04878g

Batch No

ALBEN

Table 7

Tablet	Weight	Deviation	%Deviation
1	0.6636	0.00012	0.012
2	0.6661	0.00262	0.262
3	0.6643	0.00082	0.082
4	0.6578	-0.00568	-0.568
5	0.6546	-0.00888	-0.888
6	0.6599	-0.003458	-0.358
7	0.6655	0.00202	0.202
8	0.662	-0.00148	-0.148
9	0.6658	0.00232	0.232
10	0.6546	-0.00888	-0.888
11	0.6521	-0.01138	-1.138
12	0.6536	-0.00988	-0.988
13	0.6611	-0.00238	-0.238
14	0.663	-0.00048	-0.048
15	0.6522	-0.01128	-1.128
16	0.6543	-0.00918	-0.918
17	0.6571	-0.00638	-0.638

Tablet	Weight(g) X	Deviation	% Deviation
1	0.4546	-0.00107	-0.107
2	0.451	-0.00467	-0.467
3	0.4558	0.00013	0.013
4	0.4687	0.01303	1.303
5	0.4558	0.00013	0.013
6	0.4557	0.00003	0.003
7	0.4613	0.00563	0.563
8	0.4597	0.00403	0.403
9	0.4573	0.00163	0.163
10	0.458	0.00233	0.233
11	0.4348	-0.02087	-2.087
12	0.4552	-0.00047	-0.047
13	0.4582	0.00253	0.253
14	0.4565	0.00083	0.083
15	0.4579	0.00223	0.223
16	0.4585	0.00283	0.283
17	0.4505	-0.00517	-0.517
18	0.4613	0.00563	0.563
19	0.4493	-0.00637	-0.637
20	0.4512	-0.00447	-0.447

Average weight 0.45567g

Batch No 0106G

NESBEN

Table 8

18	0.6608	-0.00268	-0.268
19	0.6544	-0.00908	-0.908
20	0.6635	0.00002	0.002

Average weight 0.66348g

Batch No **AL0701**

BENZIL

Tablet	Weight	Deviation	% Deviation
1	0.9606	-0.00305	-0.305
2	0.955	-0.00865	-0.865
3	0.9615	-0.00215	-0.215
4	0.9548	-0.00885	-0.885
5	0.9872	0.02355	2.355
6	0.9707	0.00705	0.705
7	0.9556	-0.00805	-0.805
8	0.9513	-0.01235	-1.235
9	0.9636	-0.00005	-0.005
10	0.964	0.00035	0.035
11	0.9646	0.00095	0.095
12	0.9753	0.01165	1.165
13	0.9634	-0.00025	-0.025
14	0.9715	0.00785	0.785
15	0.9701	0.00645	0.645
16	0.9568	-0.00685	-0.685
17	0.9617	-0.00195	-0.195
18	0.9578	-0.00585	-0.585
19	0.9546	-0.00905	-0.905
20	0.9707	0.00705	0.705

Average weight 0.96365g

Batch No BN NO.2

EXPEL 960 EX

Table 9

Tablet	Weight	Deviation	% Deviation

Table 10

1	0.9623	0.01115	1.115
2	0.9481	-0.00305	-0.305
3	0.9553	0.00415	0.415
4	0.9553	0.00415	0.415
5	0.9393	-0.01185	-1.185
6	0.9289	-0.02225	-2.225
7	0.9529	0.00175	0.175
8	0.9498	0.00865	0.865
9	0.9579	0.00675	0.675
10	0.9549	0.00375	0.375
11	0.9551	0.00395	0.395
12	0.9639	0.01275	1.275
13	0.9101	-0.04105	-4.105
14	0.9569	0.00575	0.575
15	0.9528	0.00165	0.165
16	0.9741	0.02297	2.297
17	0.9407	-0.01045	-1.045
18	0.9645	0.01335	1.335
19	0.9485	-0.00265	-0.265
20	0.9486	-0.00255	-0.255
Average weight		0.95115	
Batch No.	BN NO.01		
EXPEL 960 EY			

Tablet	Weight	Deviation	% Deviation
1	1.0403	-0.038225	-3.8225
2	1.0519	-0.026625	-2.6625
3	0.9881	-0.090425	-9.0425
4	1.0189	-0.059625	-5.9625
5	0.9878	-0.090725	-9.0725
6	1.0822	0.003675	0.3675
7	1.0509	-0.027625	-2.7625
8	1.0446	-0.033925	-3.3925
9	1.0513	-0.027225	-2.7225
10	1.0489	-0.029625	-2.9625
11	1.038	-0.040525	-4.0525
12	1.0158	-0.062725	-6.2725
13	1.016	-0.062525	-6.2525
14	1.0516	-0.026925	-2.6925
15	1.0242	-0.054325	-5.4325
16	1.0122	-0.066325	-6.6325
17	1.0165	-0.062025	-6.2025
18	1.0396	-0.038925	-3.8925
19	1.0404	-0.038125	-3.8125
20	1.0371	-0.041425	-4.1425
Average weight		1.078525g	
Batch No.			
WORMZAP			

Table 11

Tablet	weight(g)	Deviation	%Deviation
1	0.5621	0.0001	0.01
2	0.5582	0.004	0.4

Table 12

3	0.5562	0.006	0.6
4	0.5623	0.0001	0.01
5	0.561	0.0012	0.12
6	0.5545	0.0077	0.77
7	0.5562	0.006	0.6
8	0.5568	0.0054	0.54
9	0.5541	0.0081	0.81
10	0.5523	0.0099	0.99
11	0.5611	0.0011	0.11
12	0.5574	0.0048	0.48
13	0.5565	0.0057	0.57
14	0.5588	0.0034	0.34
15	0.5578	0.0044	0.44
16	0.5567	0.0055	0.55
17	0.5632	0.001	0.1
18	0.5571	0.0051	0.51
19	0.5645	0.0023	0.23
20	0.5624	0.0002	0.02

Average weight = 0.5622g

Batch No.

ZENTEL

Tablet	weight(g)	Deviation	%Deviation
1	0.5436	0.0016	0.16
2	0.5422	0.003	0.3
3	0.5368	0.0084	0.84
4	0.5433	0.0019	0.19
5	0.5441	0.0011	0.11
6	0.5388	0.0064	0.64
7	0.5511	0.0059	0.59
8	0.5376	0.0076	0.76
9	0.5421	0.0031	0.31
10	0.5371	0.0081	0.81
11	0.5437	0.0015	0.15
12	0.5412	0.004	0.4
13	0.5399	0.0053	0.53
14	0.5427	0.0025	0.25
15	0.5401	0.0051	0.51
16	0.5368	0.0084	0.84
17	0.5382	0.007	0.7
18	0.5384	0.0068	0.68
19	0.543	0.0022	0.22
20	0.5416	0.0036	0.36

Average weight= 0.5452g

Batch No.

ZENTEL

Table 13

Tablet	weight(g)	Deviation	%Deviation

Table 14

1	0.5711	0.0029	0.29
2	0.572	0.0038	0.38
3	0.5682	0	0
4	0.5678	0.0004	0.04
5	0.5692	0.001	0.1
6	0.5698	0.0016	0.16
7	0.5714	0.0032	0.32
8	0.5687	0.0005	0.05
9	0.5675	0.0007	0.07
10	0.5717	0.0035	0.35
11	0.5709	0.0027	0.27
12	0.5644	0.0038	0.38
13	0.5684	0.0002	0.02
14	0.5599	0.0083	0.83
15	0.5658	0.0024	0.24
16	0.5722	0.004	0.4
17	0.5649	0.0033	0.33
18	0.5676	0.0006	0.06
19	0.5731	0.0049	0.49
20	0.5689	0.0007	0.07
Average weight = 0.5682g Batch No. ALBENDAVEN			

Tablet	weight(g)	Deviation	%Deviation
1	0.5646	0.0008	0.08
2	0.5771	0.0133	1.33
3	0.5684	0.0046	0.46
4	0.5642	0.0004	0.04
5	0.5714	0.0076	0.76
6	0.5553	0.0085	0.85
7	0.5611	0.0027	0.27
8	0.5589	0.0049	0.49
9	0.5727	0.0089	0.89
10	0.5588	0.005	0.5
11	0.5586	0.0052	0.52
12	0.5536	0.0102	1.02
13	0.5623	0.0015	0.15
14	0.5641	0.0003	0.03
15	0.5641	0.0003	0.03
16	0.5728	0.009	0.9
17	0.561	0.0028	0.28
18	0.5631	0.0007	0.07
19	0.5641	0.0003	0.03
20	0.571	0.0072	0.72
Average weight = 0.5638g Batch No. ALBENDAVEN			

Table 15

Table 16

Tablet	weight(g)	Deviation	%Deviation

Tablet	weight(g)	Deviation	%Deviation
1	1.0483	0.0009	0.09
2	1.0422	0.007	0.7
3	1.052	0.0028	0.28
4	1.0461	0.0031	0.31
5	1.0461	0.0031	0.31
6	1.0511	0.0019	0.19
7	1.0451	0.0041	0.41
8	1.0431	0.0061	0.61
9	1.0506	0.0014	0.14
10	1.0501	0.0009	0.09
11	1.0601	0.0109	1.09
12	1.051	0.0018	0.18
13	1.0604	0.0112	1.12
14	1.0452	0.004	0.4
15	1.0444	0.0048	0.48
16	1.0426	0.0066	0.66
17	1.0457	0.0035	0.35
18	1.0441	0.0051	0.51
19	1.0602	0.011	1.1
20	1.0446	0.0046	0.46

Average weight =1.0492

Batch
No.

ALBEN

Table 17

1	1.0621	0.0039	0.39
2	1.07	0.0118	1.18
3	1.0654	0.0072	0.72
4	1.0624	0.0042	0.42
5	1.0666	0.0084	0.84
6	1.0571	0.0011	0.11
7	1.0641	0.0059	0.59
8	1.0681	0.0099	0.99
9	1.0622	0.004	0.4
10	1.0612	0.003	0.3
11	1.0651	0.0069	0.69
12	1.0596	0.0014	0.14
13	1.0671	0.0089	0.89
14	1.0628	0.0046	0.46
15	1.0656	0.0074	0.76
16	1.0621	0.0039	0.39
17	1.0646	0.0064	0.64
18	1.0644	0.0062	0.62
19	1.0677	0.0095	0.95
20	1.0597	0.0015	0.15

Average weight = 1.0582

Batch
No.

ALBEN

Table 18

Tablet	weight(g)	Deviation	%Deviation
1	0.7401	0.0144	1.44
2	0.7218	0.0039	0.39
3	0.7242	0.0015	0.15
4	0.7144	0.0113	1.13
5	0.7231	0.0026	0.26
6	0.7327	0.007	0.7
7	0.7235	0.0022	0.22
8	0.7341	0.0084	0.84
9	0.7371	0.0114	1.14
10	0.7255	0.0002	0.02
11	0.7268	0.0011	0.11
12	0.7199	0.0058	0.58
13	0.724	0.0017	0.17
14	0.7345	0.0088	0.88
15	0.7244	0.0013	0.13
16	0.7263	0.0006	0.06
17	0.7317	0.006	0.6
18	0.7419	0.0162	1.62
19	0.7365	0.0108	1.08
20	0.7268	0.0011	0.11

Average weight = 0.7257g

Batch
No.

WORMPLEX

Tablet	weight(g)	Deviation	%Deviation
1	0.7124	0.0019	0.19
2	0.7211	0.0068	0.68
3	0.7127	0.0016	0.16
4	0.7085	0.0058	0.58
5	0.7108	0.0035	0.35
6	0.7232	0.0089	0.89
7	0.7218	0.0075	0.75
8	0.7022	0.0121	1.21
9	0.7147	0.0004	0.04
10	0.7122	0.0021	0.21
11	0.7156	0.0013	0.13
12	0.7076	0.0067	0.67
13	0.7144	0.0001	0.01
14	0.7132	0.0011	0.11
15	0.7201	0.0058	0.58
16	0.7166	0.0023	0.23
17	0.7212	0.0069	0.69
18	0.7125	0.0018	0.18
19	0.7154	0.0011	0.11
20	0.7129	0.0014	0.14

Average weight = 0.7143g

Batch
No.

WORMPLEX

Table 19

Tablet	weight(g)	Deviation	%Deviation
1	0.9643	0.0028	0.28
2	0.9626	0.0045	0.45
3	0.9712	0.0041	0.41
4	0.9635	0.0036	0.36
5	0.9688	0.0017	0.17
6	0.9622	0.0049	0.49
7	0.9661	0.001	0.1
8	0.9686	0.0015	0.15
9	0.9723	0.0052	0.52
10	0.9708	0.0037	0.37
11	0.9701	0.003	0.3
12	0.9611	0.006	0.6
13	0.9633	0.0038	0.38
14	0.9677	0.0006	0.06
15	0.9687	0.0016	0.16
16	0.9744	0.0073	0.73
17	0.9646	0.0025	0.25
18	0.9667	0.0004	0.04
19	0.9737	0.0066	0.66
20	0.9679	0.0008	0.08

Average weight = 0.9671g

Batch No.

TANZOL

Table 20

Tablet	weight(g)	Deviation	%Deviation
1	0.9612	0.0099	0.99
2	0.9843	0.0132	1.32
3	0.9646	0.0065	0.65
4	0.9765	0.0054	0.54
5	0.9764	0.0053	0.53
6	0.9678	0.0033	0.33
7	0.9663	0.0048	0.48
8	0.9722	0.0011	0.11
9	0.964	0.0071	0.71
10	0.9695	0.0016	0.16
11	0.9623	0.0088	0.88
12	0.9745	0.0034	0.34
13	0.9741	0.003	0.3
14	0.9677	0.0034	0.34
15	0.9661	0.005	0.5
16	0.9736	0.0025	0.25
17	0.9643	0.0068	0.68
18	0.9714	0.0004	0.04
19	0.9734	0.0023	0.23
20	0.9631	0.008	0.8

Average weight = 0.9711

Batch No.

TANZOL

Table 21

Tablet	weight(g)	Deviation	%Deviation
1	0.4614	0.0021	0.21
2	0.4587	0.0048	0.48
3	0.4349	0.0286	2.86
4	0.4554	0.008	0.8
5	0.4643	0.0008	0.08
6	0.4545	0.009	0.9
7	0.4376	0.0259	2.59
8	0.4566	0.0069	0.69
9	0.4613	0.0022	0.22
10	0.4622	0.0013	0.13
11	0.4561	0.0074	0.74
12	0.4532	0.0103	1.03
13	0.4619	0.0016	0.16
14	0.4548	0.0087	0.87
15	0.4701	0.0066	0.66
16	0.4565	0.007	0.7
17	0.4483	0.0197	1.97
18	0.4622	0.0013	0.13
19	0.4641	0.0006	0.06
20	0.4488	0.0147	1.47

Average weight = 0.4635

Batch No.

NESBEN

Table 22

Tablet	weight(g)	Deviation	%Deviation
1	0.4581	0.005	0.5
2	0.4587	0.0056	0.56
3	0.4566	0.0035	0.35
4	0.4611	0.008	0.8
5	0.4534	0.0003	0.03
6	0.4524	0.0007	0.07
7	0.4581	0.005	0.5
8	0.4468	0.0063	0.63
9	0.4465	0.0066	0.66
10	0.4395	0.0136	1.36
11	0.4377	0.0154	1.54
12	0.4363	0.0168	1.68
13	0.4388	0.0143	1.43
14	0.4443	0.0088	0.88
15	0.4522	0.0009	0.09
16	0.4387	0.0144	1.44
17	0.4441	0.009	0.9
18	0.4519	0.0012	0.12
19	0.4452	0.0079	0.79
20	0.4623	0.0092	0.92

Average weight = 0.4531g

Batch No.

NESBEN