*Shittu A.O*., J. Pharm. Res. Dev. & Pract., December, 2016, Vol. 1 No. 1, P 1-11 ISSN:2579-0455

# Physicochemical Properties and Compact analysis of a new Directly Compressible Filler-Binder "Tstarac" and its Utilization in the Formulation of Ascorbic Acid Tablets

**A.O SHITTU*, A.B AFOSI**

*Department of Pharmaceutics and Industrial Pharmacy, Faculty of Pharmaceutical Sciences, University of Ilorin, Ilorin, Nigeria*

*Correspondence; Email: neobiogate@yahoo.com. GSM: +2348034388786

## ABSTRACT

An investigation into the design of a directly compressible filler/binder from two locally available raw materials is hereby reported. 'Nigeria tapioca starch' (NTS), and 'Nigeria acacia *sieberiana* gum' (NASG) were both extracted using standard methods. The resultant materials were passed through mesh 60 and were then coprocessed in isopropanol and water at ratio of 2:1. NTS and NASG were arbitrarily selected at ratio 90:10, 85:15, and 80:20 which gave flow rates of 5.6, 15.1, and 20.6 g/s; angle of repose of 32.3 $^{o}$, 30.0 $^{o}$, and 27.5 $^{o}$. compressibility index was 20.9, 17.3 and 6.0 %; while Hausner ratio was 1.21, 1.16, and 1.06, respectively.

The composite containing NTS and NASG (80:20) exhibited the best physicochemical properties and was subsequently selected for the ascorbic acid formulations. It was concluded that the coprocessed NASG and NTS have excellent compressibility and compatibility properties and can serve as cost effective excipients in conventional pharmaceutical solid dosage formulations.

**Keywords**: Ascorbic Acid Tablets, Tapioca Starch-Acacia gum Tablets, Coprocessed filler-binder, Tstarac

## INTRODUCTION

The three major processes of tablet manufacturing are by wet granulation, dry granulation, or direct compression[1]. In the past two decades, most of the pharmaceutical manufacturers have been opting for direct compression method since it involves fewer processing steps, simplified validation, elimination of heat and moisture, economic, and also improves drug stability compared with wet granulation[2]. While with dry granulation, reproducibility of the product is difficult to achieve. Hence, the current trend in the pharmaceutical industry is to adopt direct compression technology. Although simple in terms: the direct compression process is highly influenced by powder characteristics such as flowability, compressibility and dilution potential[3-6]. The attributes of directly compressible excipients are high compatibility, good flowability, good blending properties, low lubricant sensitivity, good stability and inertness[7-9].

There is no single material that is likely to exhibit all the ideal characteristics. The physicochemical properties of excipients that ensure a robust and successful process, good flowability, good compressibility, low or no moisture sensitivity, low lubricant sensitivity, and good machine ability even in high speed tabletting machines with reduced dwell times is required. Excipients with improved functionality can be obtained by developing new chemical excipients, new grades of existing materials and new combinations of same. So far, new combinations of existing excipients are an interesting option for improving excipients functionality because all formulations contain multiple excipients. A better and broader platform for the manipulation of excipients functionality is provided by combination of two or more excipients. Combination of two or more already exiting excipients in various ratios is a more effective simple process, the objective of which is to provide a synergy of functionality as well as increasing the amount of active ingredient in tablet (i.e., improved dilution capacity).

Ascorbic acid is a water-soluble vitamin, a basic need for the growth and repair of tissues in all parts of body[10]. Ascorbic acid is best known by its antioxidant activity, and the free radical scavenging[11]. Thereby it is very important for tissue recovery, collagen synthesis, and many oxidation-reduction reactions in the organism.

Ascorbic acid also takes part in the metabolism of folic acid, tyrosine, phenylalanine, iron, histamine etc. It supports the immune system, it protects blood vessels, it increases the absorption of iron in the GUT. Deficiency of ascorbic acid in the human body may cause scurvy, anemia, atherosclerotic plaques, bleeding gums, muscle degeneration, neurotic disturbances, poor wound healing[12]..

Ascorbic acid powder lacks good flow and lubrication properties.

Ascorbic acid is a high dose drug. It limits the quantity of the added excipients. Hence excipients selection for direct compression of ascorbic acid is a critical factor. Unfortunately, the physical properties of ascorbic acid indicate that it is unsuitable for direct tabletting at concentration above 60% in tabletting mixture[13-15]. Combination of excipients leads to the formation of mixtures that granulates with superior properties compared with physical mixtures of components or individual components[16-20].

Ascorbic acid is unstable in presence of moisture. Ascorbic acid is poorly compactible due to its brittleness and its strong cohesive properties. It is highly hygroscopic in nature. As a result of this its formulation is favoured by direct compression. In view of this peculiar problem of instability, couple with scarcity of directly compressible filler-binder, this research will focus on designing and formulation of a directly compressible filler-binder from Nigerian local acacia seberiana, and Nigerian cassava / tapioca starch.

## Materials

Cassava tuber *(Mannihot esculenta Crantz)* obtained from University of Agriculture Abeokuta, Ogun State, Nigeria, *Acacia sieberiana* gum obtained from Jigawa State Ministry of Agriculture, Ascorbic Acid powder (BDH Chemical Ltd. Poole, England), Starlac® (Roquette, France), Cellactose® (Meggle GmbH & Co KG

Germany), Isopropanol (Mopson Pharm. Ltd, Nigeria).

**Methods**

Extraction and Purification of Nigeria A*cacia sieberiana* (NASG) gum.

A modified method of Karayya *et al.*,[21], used by Shittu *et al.*,[22], was adopted. A 500 g of the gum was dispersed in 1 L of freshly boiled distilled water. The hydrocolloid was then filtered through 75 µm size linen. The gum was precipitated from the aqueous medium by adding slowly while stirring, 1 L of 95 % ethanol. The gum was dried in a Gallenkamp oven (model BS) at 60°C.

**Extraction of Nigeria Tapioca Starch**

A modified method of starch extraction employed by Radley, [23] was adopted.

**Table 1: Formula for Formation of Tstarac**

| | BATCH | | | | | |
|---|---|---|---|---|---|---|
| **Material** | **$B_1$** | **$B_2$** | **$B_3$** | **$B_4$** | **$B_5$** | **$B_6$** |
| **Tapioca starch (TS) (%)** | 100 | 95 | 90 | 85 | 80 | 75 |
| **Acacia gum (AG) (%)** | 0 | 5 | 10 | 15 | 20 | 25 |

Solvent used: Isopropanol and water (2:1)

**Preparation of Tstarac**

The slurry form of NTS (sieved fraction, <60 µm) was coprocessed NASG, (sieved fraction, <60 µm) using the method of Tsai *et al.*,[24]. The slurry was made by suspending the NTS in a solution of Isopropranol and freshly distilled water in ratio 2:1 respectively. NTS slurry was blended with NASG at concentrations indicated in Table 1 as a dried mass relative to NTS. The composite slurry was stirred vigorously until a semi-solid mass that easily balled was formed. The composite mass was then granulated through a 1500 µm and dried at 60 $^{o}$C until a constant weight was reached. Co-dried granules were pulverized and sized by passing through mesh size 500 µm. Both the powders and tablets were subsequently were evaluated

**Table 2: Formula for Formulation of TSTARAC-20 Placebo Tablets**

| **INGREDIENTS** | **QUANTITY** |
|---|---|
| Tstarac-20 + AA | 500 mg |
| Mg Stearate (0.5 % w/w) | 2.5 mg |
| Talc (0.5 % w/w) | 2.5 mg |
| Tablet Weight | 505 mg |

*Tstarac-20 denotes: composite containing NTS and NASG (80:20), AA denotes: Ascorbic acid*

**Compact Radial tensile strength**

The tensile strength of the normal tablets (T ) was determined at room temperature by diametral compression[26] using a hardness tester (model EH O1, capacity 500 N, Indian) and by applying the equation :

$$T = 2 F / (\pi dt )$$

Where T is the tensile strength of the tablet ($MNm^{-2}$), F is the load (MN) needed to cause fracture, d is the tablet diameter (m). Results were taken from tablets which split cleanly into two halves without any lamination. Results presented are means of three determinations.

**Disintegration Time**

Disntegration apparatus (Erweka, ZT 3, Germany) maintained at 37 $^{o}$C using three tablets in 800 ml beaker.

**Determination of dilution capacity**

Ascorbic acid was used as a model drug /active ingredient.

Model drug was blended in deferent ratios, ranging from 0 %, 5 %, 10 %, up to 50 % with Tstarac-20 ($B_5$ Table 1).

Formulations were blended by method of dilution and lubricated with 1 % magnessium stearate. Each batch was compressed for 30 seconds on single punch Carver hydraulic hand press (model, C, Carver Inc. Menomonee Falls, Wisconsin, U.S.A) at pressure load of 7.5 KN, target weight of 505 mg. Compacts were allowed to relax for 24 h post compression. Compact dimensions (diameter and thickness) were determined using a digitalized vernier caliper. Crushing strength was determined. The capacity was expressed by the dilution potential which is the maximum amount of active pharmaceutical ingredient that can be compressed with the excipient, while still obtaining tablets of acceptable quality.

**Lubricant sensitivity**

Lubricant sensitivity was determined by mixing 0.2 g of magnesium stearate (1 %w/w) with 20 g of Tstarac for the period of 5 min.

The granules without lubricant and granules with lubricant were compressed into tablets using Carver hydraulic hand press at 7.5 KN. This procedure was repeated with the same amount of magnessium stearate (1 %w/w) but the mixing time extended to 30 min.

The granules were compacted at the same compression load, crushing strength were determined and the tensile strength computed for compacts made with granules at two different mixing times.

Lubricant sensitivity ratio (LSR) was computed using the following equation:

$$LSR= (H_o – H) / H_o \times 100 \%$$

Where, LSR, $H_o$, H represent lubricant sensitivity ratio, hardness of tablet without lubricant, and hardness of tablet with lubricant respectively.

**Drug Dissolution**

The tests were conducted in 1000 ml 0.1 N HCL medium maintained at 37.0 $\pm$ 0.5 $^{o}$C at a rotation speed of 50 rpm (U.S.P XXIII).

Five ml (5 ml) of the menstrum / sample - predetermined time [5 , 10, 15, 20, 30, 45, and 60 min], and replaced with 5 ml of fresh sample for each withdrawal.

The samples were analyzed for ascorbic acid (265 nm) using U.V Spectrophotometer

(Jenway 6305). Average of three (3) readings was taken.

**Results and Discussion**

Both primary excipients were evaluated for powder properties and coprocessed at varying concentration using mixture of isopropranol and water at ratio 2:1. The various coprocessed placebo / composite filler-binders (Tstarac) were evaluated for granules and tablets properties.

.

The physicochemical properties of composite granules ratio of NTS and NAG, 90:10, 85:15 and 80:20 were in the following order: flow rate- 5.6, 15.1, and 20.6 g/s respectively; angle of repose- 32.3$^{o}$, 30.0$^{o}$, and 27.5$^{o}$ respectively; compressibility index- 20.9, 17.3, and 6.0 %, respectively; Hausner ratio- 1.21, 1.16, and 1.06 respectively (Table 3 ).

The composite containing NTS and NASG (80:20) batch B5 as shown in Table 3 with the best physicochemical properties was selected for ascorbic acid tablets

**Table 3: Physicochemical Properties of Tstarac Granules**

| Material TSAG (%) | Batch | Flow Rate (g/sec) | Angle of Repose (o) | Bulk density (g/cm$^3$) | Tapped density (g/cm$^3$) | Compressibility index(%) | Hausner's ratio |
|---|---|---|---|---|---|---|---|
| 100:0 | B1 | _ | _ | _ | _ | _ | _ |
| 95:5 | B2 | _ | _ | _ | _ | _ | _ |
| 90:10 | B3 | 5.6 | 32.3 | 0.435 | 0.526 | 20.9 | 1.21 |
| 85:15 | B4 | 15.1 | 30.0 | 0.430 | 0.497 | 17.3 | 1.16 |
| **80:20** | **B5** | **20.6** | **27.5** | **0.550** | **0.588** | **6.0** | **1.06** |

*NB: $B_1$ and $B_2$ poor flow properties*

The average granule size of Tstarac falls midway between 180 and 355 µm (Fig. 1). The granule distribution with the average located within the above range was responsible for the high flow rate, acceptable angle of repose and compressibility index.

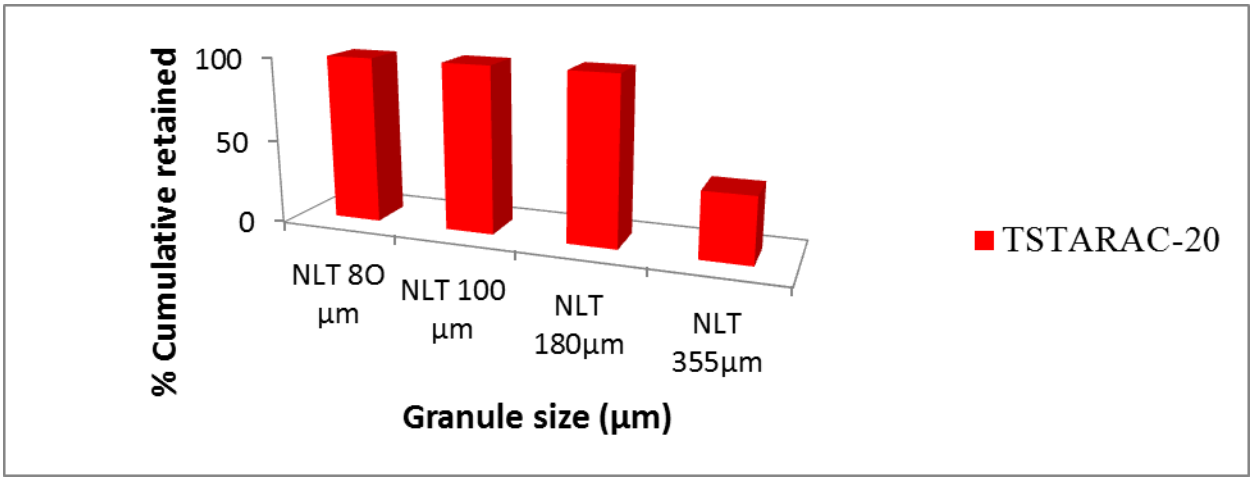



*Fig. 1 : Granule size distribution (µm) vs Cumulative retained oversize (%) of Tstsarac-20*

**Table 3: Physicochemical Properties of Tstarac Granules Compared with Standard Directly Compressible Filler-Binders**

| Material | Flow rate g/sec | Angle of Repose (o) | Bulk density g/cm$^3$ | Tapped density g/cm$^3$ | Car's index % | Hausner Ratio |
|---|---|---|---|---|---|---|
| **Tstarac-20** | 20.6 | 27.5 | 0.550 | 0.588 | 6.0 | 1.06 |
| **Starlac®** | 7.1 | 19.2 | 0.641 | 0.725 | 13.1 | 1.13 |
| **Cellactose®** | 1.84 | 24.2 | 0.443 | 0.532 | 20.1 | 1.2 |

Due to the average particle size as well as particle shape, Tstarac granules exhibits better flow property than starlac and cellactose (standard filler binders). In terms of density, Table 3 shows that starlac is denser than Tstarac which in turn is denser than cellactose.

Tstarac containing NTS (80 %) and NASG (20 %) with the best physicochemical properties was used for the formulation of ascorbic acid (AA) tablets (Table 4). The tablet target weight was 505 mg, compacted at 7.5 KN on a single punch Carver hydraulic hand press tablet machine with punch-die size of 10.5 mm. Compact evaluation of ascorbic acid tablets indicates $B_6$ tablets as more acceptable. These tablets contain Tstar ac (50%) and AA (50%) having crushing strength, disintegration time and friability values as: 115 $\pm$ 5.0 N, 8.0 min., and 1.0 % respectively

**Table 4: Compact Properties of Tstarac 20 - Ascorbic Acid Tablets**

| Batch | Material Tstarac:AA (%) | Ave. Tablet Weight (g) n=3 | Ave. Tablet Thickness (cm) n=3 | Crushing Strength (N) n=3 | Compact Density ($cm^3$) | Friability (%) n=3 | Disintegration Time (min) n=3 |
|---|---|---|---|---|---|---|---|
| 1 | 100 : 0 | 0.502±0.008 | 3.91±0.012 | 75.0±0.5 | 1.138 | 1.519 | 65:00 |
| 2 | 90 : 10 | 0.500±0.007 | 3.95±0.031 | 80.0±2.0 | 1.119 | 0.310 | 50:58 |
| 3 | 80 : 20 | 0.508±0.005 | 4.21±0.006 | 75.0±2.0 | 1.058 | 0.597 | 15:22 |
| 4 | 70 : 30 | 0.500±0.010 | 4.33±0.015 | 78.0±2.0 | 1.02 | 1.204 | 14:30 |
| 5 | 60 : 40 | 0.502±0.005 | 4.40±0.021 | 95.0±5.0 | 1.004 | 1.412 | 10:50 |
| 6 | 50 : 50 | 0.508±0.005 | 4.41±0.017 | 115.0±5.0 | 1.016 | 1.003 | 8:00 |

Table 5, shows the result of effects of prolong mixing on the tensile strength. It could be seen that addition of 1 % lubricant (magnesium stearate) mixed for minimum time (5 min.) had effect of 8.9 % reduction in compact strength, while addition of the same amount of lubricant mixing extended to 30 min. gave a reduction in compact strength of 21 %. Hence, Tstarac is moderately sensitive to prolong mixing during lubrication.

**Table 5: Lubricant sensitivity of Tstarac**

| | Compact Tensile Strength ($MN/m^2$) | Ratio of Compact Tensile Strength (LSR) % |
|---|---|---|
| **Sample** | **Tstarac** | |
| **No lubricant ($H_o$)** | 1.58±0.12 | — |
| **Lubricant 1 % 5 min. mixing (H)** | 1.44 ±0.02 | 8.9 |
| **Lubricant 1 % 30 min, mixing (H')** | 1.24 ±0.12 | 21.0 |

The figure 2[a] and 2[b] below shows compact tablet of ascorbic acid after 48 hours storage.

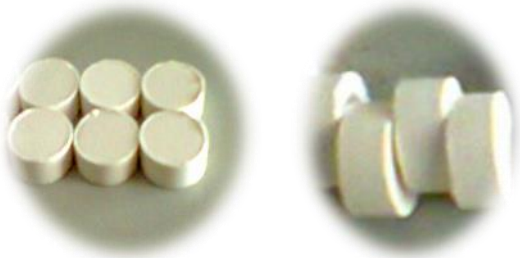


*Figure 2[a,b]: Ascobic acid tablets formulated with Tstarac*

**Dissolution of Drug**

As shown in table 6, tablets of Tstarac-AA containing 50 % API (250 mg ascorbic acid), the $T_{90\%}$ was found to be 15 min and the dissolution efficiency (DE) was also determined to be 8 min. The tablets released 100 % of its active ingredient in 18 min. For cellactose®-AA containing 50% API (standard), $T_{90\%}$ was found to be 12 min. and the dissolution efficiency (DE) was found to be 7 min. The tablets released 100 % of its active ingredient in 20 min.

**Table 6: Summary of Tstarac-Ascobic Acid Tablets**

| Tablet Parameters | Tstarac-AA (50:50) | Cellactose®-AA (50:50) | Starlac®-AA (50:50) |
|---|---|---|---|
| **Tablet weight (mg±SD)** | 0.508±0.005 | 502 ± 1 | 501 ± 2 |
| **Amount of API (mg)** | 250 | 250 | 250 |
| **Crushing strength (N)** | 115±0.9 | 75.0 ± 3.0 | 30.0 ± 2.0 |
| **Friability (%)** | 1.003 | 0.21 | 100 |
| **Disintegration Time (Min.)** | 8:00± 1.00 | 0.57±0.03 | ND |
| **Dissolution Time (Min) $T_{90\%}$** | 15 | 12 | ND |
| **Content Uniformity (%)** | 98.0 | 99.2 | ND |

ND : No data.

**Summary and Conclusion**

For conventional tablets, T90% is stipulated to not greater than 45 min, British Pharmacopoiae standard. Tstarac-20 batch 6, containing 50 % API ( 250 mg) disintegrated in 8 min., have acceptable crushing strength, 115±5.0 N, $T_{90\%}$ 15min.

The purpose of this present study was to develop and formulate a directly compressible filler-binder with high functionality from two local materials, "NASG and NTS employing solvent evaporation technique. The formulated Tstarac granules were incorporated into tablet dosage form at dilution potential (DP) upto 50% in respect of AA.

In conclusion, coprocessed NASG and NTS have excellent compressibility and compactibility, cost effective and possess the advantage of being naturally sourced, could prospectively be employed for formulating conventional pharmaceutical solid dosage forms.

References


1. Aulton ME. Pharmaceutics, the Science of Dosage Forms Design,( 1988) International Student Edition, Churchill Livingstone, 304.
2. Steinberg M, Blecher L.(2001). From inactive ingredients to pharmaceutical excipients Pharmaceutical Technology. 25:62–64.
3. Jon Gabrielsson, Nyström Å.,(2000). Multivariate Methods in Developing an Evolutionary Strategy for Tablet Formulation. Drug Development and Industrial Pharmacy. 26(3):175-296.
4. Karhill PG, Sherif Badaway, (1990). Development of Directly Compressible Ascorbic Acid Tablet Using Novel Excipients. Drug Development Industrial Pharmacy. 64:27-34.
5. Alderborn, G., Wikberg, M, (1991). Compression characteristics of granulated materials. IV. The effect of granule porosity on the fragmentation propensity and the compactibility of some granulations. International Journal of Pharmaceutics 1991;69:239–253.
6. Rang Kanchan, Sherif Badaway,(1995). Influence of powder characteristic such as flowability, compressibility and dilution potential on direct compression process Drug Development and Industrial Pharmacy; 21(3):361-368.
7. Sitton E, Lewis CJ. (1964). Attributes of directly compressible excipients Journal of Pharmacy Pharmacology,;16(Suppl.):111T.
8. Levy G, Gumtow RH.( 1963). Effect of certain Tablet Formulation Factors on Dissolution Rate of the Active Ingredient. "Tablet Lubricants". 52:1139-44. Journal Pharmaceutical Sciences,; 52:1139.
9. Shah C, Mlodozniec AR.( 1977). Attributes of Pharmaceutical Excipients affecting functionalities

of Tablet Formulations. Journal of Pharmaceutical Sciences,; 66:1377.

10. Roe, D.A., Campbell, T.C., (Eds), (1984). Drug and Nurients, "The Interactive Effects, Vol. 21. Marcel Dekker, New York. 21:225 – 295.

11. Heber D (2007). PDR for Herbal Medicines 4th edition. Thoson Healthcare, Montvale.

12. Iqbal K, Khan A, Muzaffar, A (2004). Biological significance of ascorbic acid (Vitamin C) in human health – A review. Parkistan Journal of Nutrition. 3(1): 5 – 13.

13. Nystrom C, Glazer, M, (1985). Studies on direct compression of tablets. International Journal of Pharmacy. 23: 255 – 263.

14. Alderborn G, Pasanen K., (1985). The influence of the particle size of a dry binder on the mechanical strength of tablets. International Journal of Pharmacy. 23:79 – 86.

15. Nystrom C, Mazur J., (1982). Studies on direct compression of tablets II. International Journal of Pharmacy. 10:209 – 218.

16. Alderborn G, Nystrom C., (1996). "Pharmaceutical Powder Compaction Technology". Marcel and Dekker Series. 419 – 487.

17. Hans Leuenberger. (2000). Composite granulates compare with mixture of excipients. European Journal of Pharmaceutics and Biopharmaceutics. 49: 151 – 159.

18. Picker K. M., (1999). The use of carrageenan in mixture with microcrystalline cellulose and its functionality for making tablets. European Journal of Pharmaceutics and Biopharmaceutics. 48:27 – 36.

19. Kenta G, Hisakazu S, Kazumi D, and Yorinobu Y., (1999). Pharmaceutical Evaluation of Multipurpose Excipients for Direct Compression Tablet Manufacture: Comparisons of the Capabilities of Multipurpose Excipients with Those in General Use. Drug Development and Industrial Pharmacy. 25 (8): 869 – 878.

20. Tsuimin T, Jen-Sen W, Hsiu-O H, and Ming-Thau S., (1998). Modification of physical characteristics of microcrystalline cellulose by codrying with β-cyclodextrins. Journal of Pharmaceutical Sciences. 31:576.

21. Karayya, M.S., Balba, S.L., and Afofi, M.S.A., (1971). Investigation of the carbohydrate contents of certain mucilaginous plants. Planta medica. 20:14 – 23.

22. Shittu, A.O., Oyi, A.R., and Onaolapo, J.A.,(2007)."Investigation into the suitability of Acacia sieberiana gum as a matrix device in chloroquine phosphate and metronidazole tablets". M.Sc.

Pharmaceutics Thesis, Ahmadu Bello University Zaria.

23. Grace, M. R. Cassava Processing, (1977). Plant Production and Protection series No. 3 FAO,Rome.

24. Tsai, T.,Wu, J, Ho, H., and Sheu, M, Modifcation of Physical Characteristics of Microcrystalline Cellulose by Codrying with β-cyclodextrin, Journal of Pharmaceutical Sciences. 87: 117-122.

25. Kawakita, K., and Ludde, K. H, (1970/7). Some considerations on power compression equations. Powder Technology. 14: 61 – 68.

26. Fell, J.T., Newton, J.M.(1970). Determination of tablet strength by the diametral compression test. Journal of Pharmaceutical Sciences. 59: 688– 691