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DESIGN, FORMATION AND EVALUATION OF A CO-DRIED DIRECTLY COMPRESSIBLE EXCIPIENT "TSAG-15" AND ITS UTILIZATION IN THE FORMULATION OF A RAPID RELEASE-MOUTH DISINTEGRATING ASCORBIC ACID TABLETS

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Rapid Release, Mouth Disintegrating Tablets, Ascorbic Acid Tablets, Tapioca Starch-Acacia gum Tablets, Coprocessed excipient-TSAG 15

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ABSTRACT:A research was conducted to design a directly compressible filler binder characterized with rapid release and mouth disintegrating. Acacia gum was obtained from local source and was purified using a standard method. Tapioca starch was also extracted from cassava tuber using a standard method. Both primary excipients were evaluated for power properties and coprocessed at varying concentration using mixture of isopropranol and water at ratio 2:1. The various coprocessed placebo composite filler-binders (TSAG) were evaluated for granules and tablets properties. The composite containing 85 % tapioca starch and 15 % acacia gum (TSAG-15) have excellent flow rate, angle of repose, compressibility index and Hausner's ratio: 25 g/s, 30^{o}, 17.3 %, and 1.2 respective. The placebo tablets of this composite was characterized with high functionality, when compressed at 6.5 KN, gave crushing strength of 102 N, friability of 1.12 %, disintegration time of 5-6 min. Ascorbic acid tablets compacted with the composite filler binder having 80 % TSAG-15 and 20 % ascorbic acid gave good compacts with average crushing strength of 60±0.5 N, friability of 1.2 % and average disintegrating time of 1 min 48 s. Since the compacts possessed acceptable tablet quality and met the condition for a mouth disintegrating tablet by disintegrating within 3 min. TSAG-15 is therefore acceptable for formulation of fast release, mouth disintegrating tablets of highly soluble active ingredients.

INTRODUCTION: Amongst various route of drug delivery, oral route has being adjourned as the most preferred and more acceptable to patients and the clinician. However, some of the setback for per oral administration of drugs include: hepatic first pass metabolism and enzymeatic degradation within the GI tract which prohibit oral administration of some classes of drugs such as peptides and proteins, bed ridden, children and old age patients often face swallowing problems leading to poor patient compliance.

In view of these, other absorptive mucosa has been considered as potential sites for drug administration.

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Tran's mucosa routes of drug delivery such as the mucosal linings of the nasal, rectal, vaginal, ocular and oral cavity, offer distinct advantages over per oral administration for systemic drug delivery. These advantages include possible bypass of first pass effect, avoidance of pre systemic elimination within the GI tract and a better enzymatic flora for drug absorption [1].

The buccal region offers an attractive route of administration for systemic drug delivery. The mucosa has a rich blood supply and provides rapid absorption for drugs than oral route. Therefore, the oral mucosa may be a potential site for both conventional and controlled or sustained drug delivery.

The permeabilty of the oral mucosa is low; hence the oral could be utilized for potent drugs which are required in small doses [2].

Orodispersible tablets are prepared which when placed on tongue disintegrates within seconds and the drug dissolves or get dispersed in saliva[3]. As no water is needed to administer these tablets, these offer an advantage for travelers who may not have access to water. The technologies employed for preparation of orodipersible tablets include: lyophilization[4], moulding[5], direct compression [6], cotton candy process [7], spray drying [8], sublimation [9] and nanonization[10]. These techniques are based on the principles of increasing porosity and/or addition of superdisintegrant and water soluble excipients in the tablets [11].

Plant products nowadays are widely used as a substitute to synthetic products due to ease of local available, lower prices as compared to synthetic products, biocompatible, biogradable and environment friendly nature. Locust bean gum also called carob bean gum extracted from the seeds of the Carob tree (Ceretoniasiliqua), mostly found in the Mediterranean regions. Locust bean gum has been widely used in food industry as a thickening and gelling [12]. Recently it has been established as a potential superdisintegrant in orodispersible tablets [13]. Owing to extensive swelling properties and superdisintegrant action of locust bean gum, it was used as superdisintegrant in orodispersible tablets containing taste masked microspheres of ofloxacin [14].

Hence, this research work planned to design, formulate and evaluate a directly compressible excipient characterized with rapid release and disintegrate within 3 min in the mouth using a composite excipient TSAG-15 made from acacia gum and tapioca starch..

Materials: Cassava tuber *(Mannihotesculentacrantz)* obtained from University of Agriculture Abeokuta, Ogun State, Nigeria, *Acacia sieberiana* gum obtained from Jigawa State Ministry Agriculture and Forestry Phloroglucinol, iodine, xylene, Starlac (Roquette, France), Cellactose

(Meggle, Germany), microcrystalline cellulose (Avicel 101).

Methods:

Extraction and purification of *Acacia sieberiana* gum: The method of Karayya*et al*[15], used by Shittu*et al* [16], was adopted. One kilogram of the gum was dispersed in 2 L of hot 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, 5 L of 95 % ethanol. The gum was dried in a Gallenkamp oven (model BS) at 60°C.

Extraction of Tapioca Starch: Cassava tubers were washed and peeled to remove the outer skin and rind with the aid of a handy stainless knife. The peeled tubers were washed with freshly distilled water and rasped.

The rasp consists of a sheet of metal plate perforated with nails, clamped around a stainless bucket with the protrusions facing outwards. The tubers were then manually rasped to a pulp on the stationary grater (which is the metal plate perforated by nails). Water was applied in small quantities continuously to the rasper. The process was continued until the whole tubers were turned into a fine pulp in which most but not all of the starch granules were released.

After rasping, pulp from the sump was then pumped on to a nylon fastened /clamped around a stainless bucket. A small spray of water was applied to assist the separation of starch granules from their fibrous matrix and to keep the screen mesh clean while water was added, the mass were turned manually to aid the release of the granules.

Starch granules carried with the water fall to the bottom of the bucket in which the sieve was placed. The starch milk was then allowed to sediment, by standing for a period of 8 h. The starch settled at the bottom of the bucket and the supernatant liquor decanted.

The sediment / fine granules were centrifuged. After the removal of free water from the starch, cake was obtained. The starch cake was then crumbled into small lumps (1-3 cm) and spread out in thin layers on stainless trays and air dried for 120 h [17, 18].

The slurry form of tapioca starch (TS) (sieved fraction, <75 µm) was coprocessed acacia gum (AG), (sieved fraction, <75 µm) using the method of Tsai *et al*[19]. The slurry was made by suspending the TS in a solution of Isopropranol and freshly distilled water in ratio 2:1 respectively. TS slurry was blended with AG at concentrations indicated in **Table 1** as a dried mass relative to TS. The composite slurry was stirred vigorously with a stirrer until a semi-solid mass easily ball was formed. The composite mass was then granulated through a 1500 µm and codried at 60^{o}C until a constant weight was reached. Codried granules were pulverized and sized by passing through mesh size 500 µm. The powder and tabletting properties of the codried products were evaluated.

TABLE 1: FORMULA FOR FORMATION OF TSAG

Material	BATCH					
	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)

Compactibility: The various batches of coprocessed tapioca starch (TS) and acacia gum (AG) "TSAG", (Table 1) were compressed on a single punch Erwekatabletting machine (Erweka, AR 400. Germany) fitted with 10.5 mm diameter flat faced punch and die. Tablet target was 505 mg (**Table 2**), and pressure load used range from 7.5 KN.

TABLE 2: FORMULA FOR FORMULATION OF TSAG-15 PLACEBO TABLETS

INGREDIENTS	QUANTITY
TSAG-15	500 mg
Mg Stearate (0.5 % w/w)	2.5 mg
Talc (0.5 % w/w)	2.5 mg
Tablet Weight	505 mg

Moisture content: The moisture content (MC) of the granules were determined by weighing 100 g of the powder after which it was heated in an oven at a temperature of 105 °C until a constant weight was obtained.The moisture content was then calculated with the following formula:

$$MC = (1 - W_t/W_0) \times 100 \quad \ldots\ldots(2)$$

Where W_t and W_0 represent weight of powder after time 't' and the initial weight before heating respectively.

Determination of Flow Rate and Angle of Repose: Angle of repose was determined using a standard method and equation 3 bellow.

$$\theta = \tan^{-1}(h/r) \quad \ldots\ldots(3)$$

The flow rates were determined with the aid of Erweka flowability tester (model GDT, Germany).

Densities:

Bulk and Tap density: These parameters were determined by weighing 50 g quantity of each granule/powder and pouring into a 100 ml measuring cylinder. The volume (V_o) was recorded as the bulk volume. The total weight of the granule/powder was noted. The bottom of the cylinder was raised 10 cm above the slab and made to fall on the platform continuously for 100 taps. The volume of (V_t) of the granule was recorded, and this represents the volume of the granules minus the voids and is called the tapped volume. The final weight of the powder too was recorded as the tapped weight[20].

The bulk and tapped densities were calculated as:

$B_d = W/V_o$……..(4)
$B_t = W/V_t$……....(5)

Where, B_d and B_t, are bulk and tapped density respectively, and W, is the weight of the powder (50 g).

The results presented are the mean of three determinations.

Carr's Index:

Carr's Index (CI) = $(\rho^T - \rho^o)/\rho^o$ x 100 % ……(6)

Where ρ^o is the poured or bulk density and $\rho^k$is the tapped density.

Evaluation of Tablets:

Weight variation limit test: The weights of 10 tablets were determined individually and collectively on a Metler balance (Denver, XP-300, USA). The mean weight, percentage (%) deviation from the mean and standard deviation were calculated.

Thickness of Tablets: The thickness of the tablets was measured with the aid of micrometer screw gauge. Five tablets were selected randomly and the thickness for each was measured and the mean value determined.

Hardness of Tablets: Crushing strength was determined using an electronic/digitalized tablet hardness tester (model EH O1, capacity 500 N,Indian).

Friability: The friability test was performed for the tablets formulated in a friabilator (Erweka, TA 3R). The weight of 10 tablets was determined on a Metler balance (Denver, XP - 300, U.S. A). The tablets were placed in the friability and set to rotate at 25 rpm for 5 min after which the tablets were de-dusted gently and their weight determined. The difference was calculated and the percentage loss in weight and hence the value of the friability was calculated.

Compact Volume: The volume of a cylindrical tablet having radius 'r' and height 'h' is given by the following equation

$Vc = h\pi r^2$ ……(7)

Compact density: The compact density of a tablet was calculated from the following equation

Compact density (ρ) = Weight of tablet / Volume of tablet ……(8)

Compact Radial tensile strength: The tensile strength of the normal tablets (T) was determined at room temperature by diametral compression[21] using a hardness tester (model EH O1, capacity 500 N, Indian) and by applying the equation:

$T = 2 F / (\pi dt)$……(9)

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. All measurements were made in triplicate, and the results given are the means of several determinations.

Compression pressure: This was derived from the relationship between the applied pressure and surface area.

CP = Applied force / Surface area of tablet ……(10)

Disintegration Time: Disintegration apparatus (Erweka, ZT3, Germany) was employed. Three tablets were placed in each compartment of the disintegration basket which was lowered into a glass beaker (1 L capacity) filled with deionized water to 800 ml mark and in turn was placed in a water bath maintained at 37°C. The time taken for the disassociated tablet particles to pass through the mesh was recorded as the disintegration time. Average of three readings was taken as the disintegration time.

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 TSAG-15 and TSAG-20.Formulations were blended by method of dilution and lubricated with 1 % magnesium 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 500 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 using an electronic/digitalized tablet hardness tester (model EH O1, capacity 500 N,Indian). A relationship between amount in percent (%) of model drug added to the formulation and the tensile strength will be generated.

In general, the capacity was expressed by the dilution potential as being an indication of the maximum amount of active pharmaceutical ingredient that can be compressed with the excipient, while still obtaining tablets of acceptable quality (that is, acceptable crushing strength average of 60 N, friability, < 1.0 %, good disintegration time < 15 min, and must meet the requirement of U.S.P weight variation limit test).

RESULTS AND DISCUSSION:

Physicochemical Properties of Granules:

Granule size distribution: Fig.1 showed the granule size distribution range as: ≤ 355 µm - ≥ 80 µm. This range was responsible for the flow characteristics and other granules properties of TSAG-15.

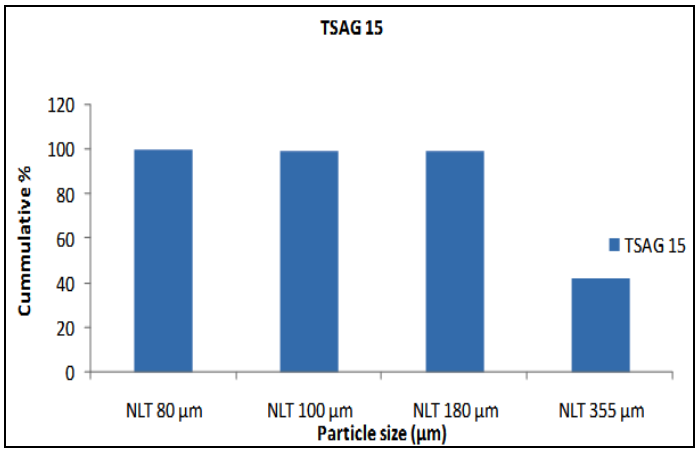

FIG. 1: GRANULE SIZE DISTRIBUTION (µm) VS CUMMULATIVE RETAINED OVERSIZE (%) OF TSAG-15

Flow Rate: From **table 3** the batches had flow rates ranging from 15.11 to 20.67 g/sec. A good flow property is essential for compression of tablet because it ensures proper flow of granules from hopper into the die cavity.

From the result obtained, the flow rate increased with increase in percentage of acacia gum.

Angle of Repose: The angle of repose is also used to predict the flowability of powders and provides a reliable index of powder flow. The result from table 3, showed an angle of repose of 30.0^{o} for TSAG (85:15) indicating good free flow properties. Mild cohesive powders have angle of repose between 40^{0} and 60^{0}, very cohesive powders forms an angle of repose closer to 90^{0}, while free flowing powders give an angle 35^{0} or less respectively. Generally, the higher the values of the angle of repose for a powder the more cohesive it is.

Compressibility Index: Powders with compressibility index of 38-40 % are very cohesive and poorly flowable. Values above 20 % do not indicate very good flow behaviors.

TSAG-15, from **table 3**, gave compressibility index of 17.3 %, thus indicating good flow properties.

Moisture Content: The TSAG-15 had percentage loss on drying of 12 % this agrees with the fact that granules for compression must have minimum moisture content which varies with the material in order to compress satisfactorily.

Hausner's Ratio: It is a measure of interparticulate friction in the powder[22]. It is useful in prediction of powder flow properties. The TSAG-15 gave Hausner's ratio 1.16. Good flowability has ratio of 1.2 (Hausner's, 1967), while more cohesive and less free flowing powders have Hausner's ratio greater than 1.6. The results obtained in table 3 indicate that the powder have low inter particulate friction and thus good flowing and less cohesive.

TSAG-15 Tablets (Placebo): From **table 4**, the tablets compressed at 6.5 KN have crushing strength of 102 N, friability, 1.12 %; and disintegration time, 5-6 min.**Fig. 2** showed the granule distribution of TSAG-20. The granules retained on sieve size 355 µm (not more than 500 µm) constitute 40 %, while the remaining granules (NLT 80 to 180 µm) account for the remaining 60 %.

TABLE 3: PHYSICOCHEMICAL PROPERTIES OF TSAG GRANULES

Material TSAG (%)	Batch	Flow Rate (g/sec)	Angle of Repose (^{0})	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

TABLE 4: COMPACT PROPERTIES OF TSAG-15 -ASCORBIC ACID COMPRESSED TABLET

Batch	Material TSAG : AA (85:15) : AA (%)	Ave. tablet weight (g) n=3	Ave. tablet thickness (cm) n=3	Crushing strength (N) n=3	Compact density g/cm^3	Friability (%) n=3	Disintegration time (min) n=3
1	100 : 0	0.497± 0.005	0.403±0.025	80 ± 0.0	1.0899	0.940	1:23
2	90 : 10	0.502± 0.006	0.409±0.01	82 ± 0.3	1.087	1.077	1:32
3	**80 : 20**	0.496± 0.0055	0.427±0.027	**60 ± 0.5**	1.027	**1.183**	**1:48**
4	70 : 30	0.499± 0.006	0.460±0.015	50 ± 0.1	0.96	0.888	9:49
5	60 : 40	0.501± 0.007	0.521±0.027	27 ± 0.3	0.849	1.524	24:16
6	50 : 50	0.494± 0.005	0.590 ± 0.01	20 ± 0.0	0.805	2.009	27:09

TABLE 5: COMPACT PROPERTIES OF TSAG 20-ASCORBIC ACID TABLETS

Batch	Material TSAG:AA (80:20):AA(%)	Ave. Tablet Weight (g) n=3	Ave. Tablet Thickness (cm) n=3	Crushing Strength (kgf) 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	7.5±0.5	1.138	1.519	3:22
2	90 : 10	0.500±0.007	3.95±0.031	8.0±1.0	1.119	0.310	11:42
3	80 : 20	0.508±0.005	4.21±0.006	7.5±0.9	1.058	0.597	14:22
4	70 : 30	0.500±0.010	4.33±0.015	7.8±1.0	1.02	1.204	38:42
5	60 : 40	0.502±0.005	4.40±0.021	9.5±0.5	1.004	1.412	50:58
6	50 : 50	0.508±0.005	4.41±0.017	11.5±0.9	1.016	1.003	1:20:41

Compression force = 5 MT. Diameter of the punch= 12mm

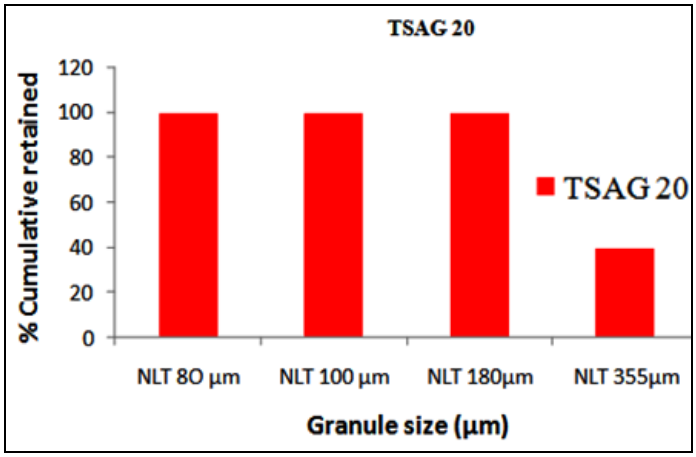

FIG. 2: GRANULE SIZE DISTRIBUTION (µm) VS CUMULATIVE RETAINED OVERSIZE (%) OF TSAG-20

Fig. 3 showed that as the ascorbic acid content increases the tablet thickness increases. This is an indication that the tablet density decreases with increase in amount of ascorbic acid (AA) in both TSAG-15 and TSAG-20.

The increase in tablet thickness is higher in TSAG-15 than TSAG-20. This showed that tablets of TSAG-20 AA are more compact than those of TSAG-15 AA.

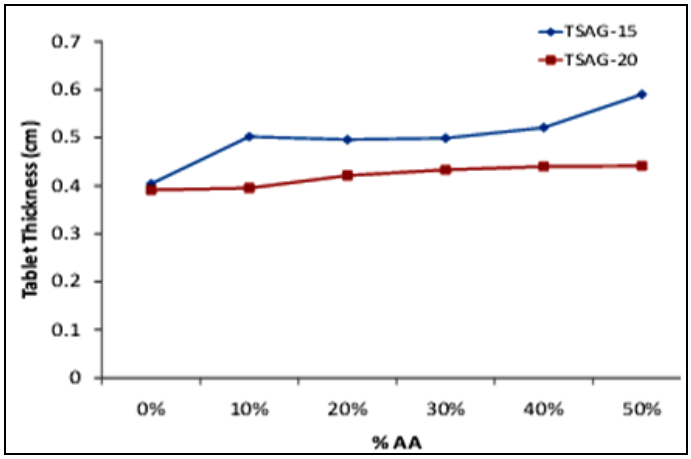

FIG. 3: TABLET THICKNESS (cm) VERSUS AMOUNT (%) OF ASCORBIC ACID IN THE COMPACTS OF TSAG-15 AND TSAG-20

Fig.4 showed that compact density of both TSAG-15 and TSAG-20 AA decreased with increased in AA content. But the decrease is more pronounce in TSAG-15 than in TSAG-20 AA. The reason could be attributed to the higher content of acacia gum (a binder) in TSAG-20 resulting in better compact than TSAG-15. The higher the binder content the higher the compact density.

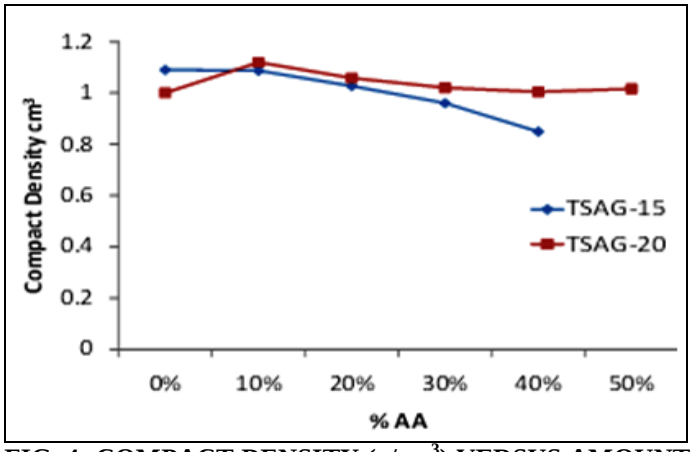

FIG. 4: COMPACT DENSITY (g/cm^3) VERSUS AMOUNT (%) OF ASCORBIC ACID IN COMPACTS OF TSAD-15 AND TSAG-20

Fig.5 showed that the crushing strength (hardness) of TSAG-20 rises a little from 7.5±0.5 N to 8.0±1.0 N for compact containing 0% to 10% AA respectively. The crushing strength varied from 8.0±1.0 N to 7.5±0.9 N for compacts containing 10% to 30% of AA respectively. There was a significant rise in crushing strength from 7.5±0.9 N, to 11.5±0.9 N for compacts containing 40% to 50% AA respectively.

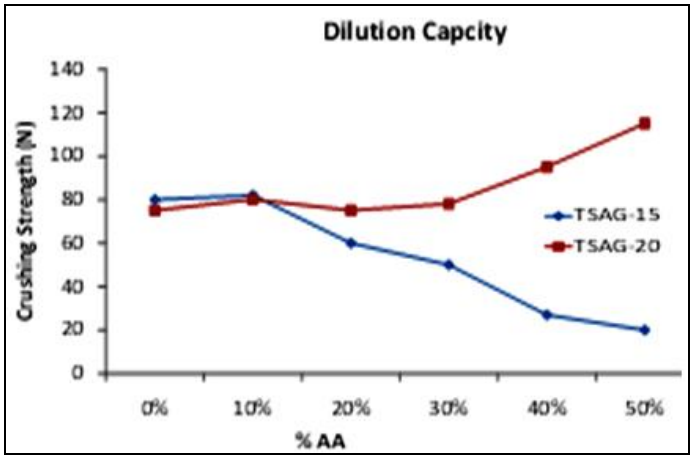

FIG. 5: CRUSHING STRENGTH (N) VERSUS AMOUNT (%) OF ASCORBIC ACID IN COMPACTS TSAG-15 AND TSAG-20

The graph of TSAG-15 showed that the compacts containing 20% AA and 80% TSAG-15 have acceptable crushing strength of 60±0.5 N.**Fig.6** showed disintegration (DT) time with increase in AA content. The TSAG-20 AA compact showed higher DT ranging from 3.22 min to 14.22 min for compacts containing 0% to 20 % and, 14.22 min to 50.58 min for compact containing 20% to 40 % and 1.21 min for compacts containing 50% AA.While for TSAG-15, the graph showed the DT to be 1.23 min to 1.48 min for compact containing 0% to 20% AA, 1.48 min to 24.16 % for compacts containing 20% to 40%and 27.09 min for compact containing 50% AA.

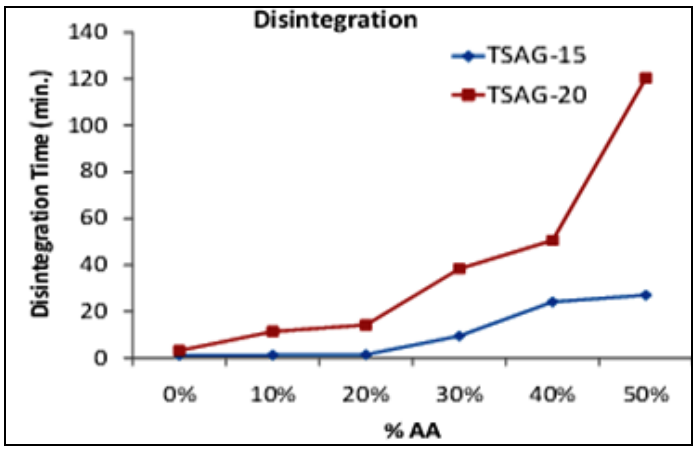

FIG. 6: DISINTEGRATION TIME (min) VERSUS AMOUNT OF ASCORBIC ACID (%) IN TSAG-15 AND TSAG-20

The TSAG-20 possessed longer DT due to higher content of acacia gum (binder) than TSAG-15.A short disintegration time indicates that the bond are easily broken while longer disintegration time is due to formation of many strong bonds which takes longer time to break.

TSAG-20 AA containing 40 % to 50 % AA can therefore be employed for extended release non-disintegrating tablets, while TSAG-15 AA containing 20 % AA (i.e., 100 mg AA) can be employed for fast release oral tablets based on average tablet hardness of 60±0.5 N, friability, 1.18 % and average DT of 1.48 min.

Dissolution of Drug: From **fig. 7**, for the TSAG-15 ascorbic acid containing 20 % API (100 mg ascorbic acid) the $T_{90\%}$ was found to be 8 min and the dissolution efficiency (DE) was also determined to be 3.5 min. The tablets released 100 % of its active ingredient in 10 min.

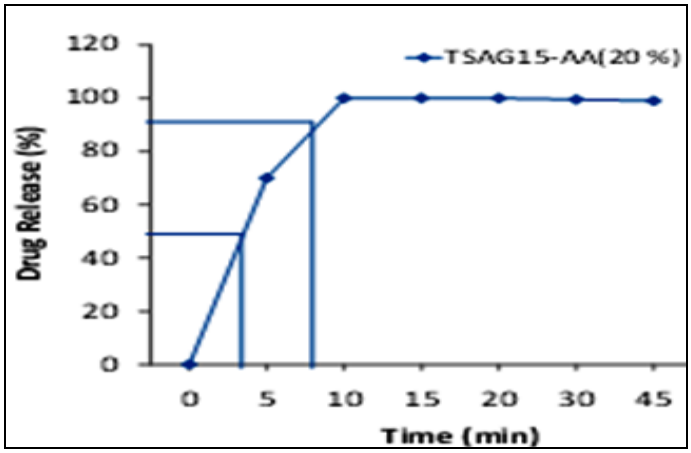

Fig. 7: DRUG RELEASE (%) VERSUS TIME (MIN) FROM ASCORBIC ACID TABLET CONTAINING 80% TSAG-15 AND 20% ASCORBIC ACID

SUMMARY AND CONCLUSION: For mouth disintegrating tablets, several works stipulate a maximum of 3 min. disintegration time, as stipulate by EuropeanPharmacopoeial standard.Batch 3, containing 20% API (100 mg) disintegrated in 1 min 48 sec. and has acceptable crushing strength, 60 N and friability (1.2%) .

TSAG 15-AA Tablets: Acceptable/good compacts, crushing strength, 60 N, friability, 1.2%, disintegration time, 1 min, 48 sec. (< 3 min), hence could be used as Fast Release, Mouth Disintegrating Tablet, while TSAG-20 AA containing 40% to 50% AA can therefore be employed for non-disintegrating tablets extended release oral tablets[23].

REFERENCES:

1. Bruschi, Marcos L, and Freitas D, Osvaldo. Oral bioadhesive drug delivery systems. Drug.Dev. Ind. Pharm. 2005; 31: 293-310.
2. Vyas S.P, and Khar K.R. Controlled drug delivery concepts and advances, New Delhi: VallabhPrakashan; first edition 2002; 292.
3. Hirani J, Rathod D. and Vadalia K. Orally disintegrating tablets: A review. Trop J. Pharm. Res. 2009; 8: 161 – 172.
4. Seager H. Drug – delivery products and the Zydis Fast-dissolving dosage form. J. Pharm. Pharmacol. 1998; 50: 375-382.
5. Pebley W.S, Jager N.E, and Thompson S.J. Rapidly disintegrating tablet. United States Patent 5,298,261
6. Watanabe Y. New compressed tablet rapidly disintegrating in the mouth using crystalline cellulose and a disintegrant. Biol. Pharm. Bull. 1995; 18: 1308-1310.
7. Myers G.L, Battist G.E, and Fuisz R.C. Process and apparatus for making dissolving Dosage units and product there from. PCT. Patent W.O 95/34293-A1.
8. Allen L.V and Wang B. Process for making a particulate support matrix for making a rapidly dissolving tablet. United State Patent 5,587,180.
9. Koizumi K.I, Watanabe Y, Morita K, Utoguchi N, and Matsumoto M. New method for preparing high porosity rapidly saliva soluble compressed tablets using mannitol with camphor a subliming material. Int. J. Pharm. 1997; 152: 127-131.
10. Khan S, Kataria P, Nakhat P, and Yeole P. Taste masking of Ondensetron Hydrochloride by polymer carrier system and formulation of rapid disintegrating tablets. AAPS PharmSci. Tech. 2007; 8:46-57.
11. Fini A, Bergamante V, Ceschel G.C, Ronchi C, and Moraes C.A. Fast dispersible/slow releasing ibuprofen tablets. Eur. J.Pharm.Bio. 2008; 69:335-341.
12. Cheng H. Xanthan gum and locust bean gum in confectionary use. United States Patent 4, 219,582.
13. Malik K, Arora G, and Singh I. Locust bean Gum as superdisintegrant- Formulation and Evaluation of Nimesulide Orodispersible Tablets. Polym. Med. 2011; 41: 17-28.
14. Covino J.M, Cummings M, Smith B, Benes S, Draft K, and William M. Comparison of Ofloxacin and Ceftriaxone in the Treatment of Uncomplicated Gonorrhea caused by Penicillinase-Producing and Non-Penicilinase-Producing Strains. Antimicrob Agents Chemother. 1990; 34: 148-149.
15. Karayya M.S, Balba S.I, and Afofi M.S.A., PlantaMedica. 1971, 20, 14 – 23.
16. Shittu, A.O., Oyi, A.R., and Onaolapo, J.A., "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, 2007.
17. Grace, M. R. Cassava Processing. Plant Production and Protection series No. 3 FAO, Rome, (1977)
18. Radley, J. A. Starch Production Technology. Applied Science Publishers, London, p. 587 (1976).
19. Tsai, T.,Wu, J, Ho, H., and Sheu, M , Modifcation of Physical Characteristics of Microcrystalline Cellulose by Codrying with β-cyclodextrin, J.Pharm. Sci., 87: 117-122, 1998.
20. Kawakita, K., and Ludde, K. H. Some considerations on power compression equations. Powder Technology, 1970/7; 14: 61 – 68.
21. Fell, J.T., and Newton, J.M. Determination of tablet strength by the diametral compression test. Journal of Pharmaceutical Sciences, 1970; 59: 688 – 691.
22. Hausner H. Friction conditions in a mass of metal powder. Int. J. Powder Metal 1967: 3.
23. Malik, K, Arora G, and Singh I. Locust bean Gum as Superdisintegrant – Formulation and Evaluation of Nimesulide Orodispersible Tablets. Polym Med, 2011; 41: 17-28.

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