Research Article

Formulation and Evaluation of *Allium Sativum* Tablets for Improved Oral Delivery

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ABSTRACT

In view of the widespread use of *Allium sativum* (garlic) in the treatment of diseases, there is an important need for standardization and quality control in order to enhance their efficacy and improve patient compliance. The aim of the study was to formulate *Allium sativum* tablets and to evaluate the properties of the tablets. Garlic tablets were prepared by wet granulation using acacia, gelatin and sodium carboxymethylcellulose (SCMC) as binders at concentrations of 2, 4, 6 and 8 % w/w. The tablets were evaluated using both official and non official tests. Also the phytochemical constituents of garlic were studied. The results showed that tablets weight ranged from 301.20 ± 0.40 to 312.40 ± 2.11 mg. The crushing strength of the tablets was affected by the binder type and concentration used. The order of tablets hardness in increasing order is: SCMC > acacia > gelatin. Increase in binder concentration significantly caused an increase in the crushing strength of the tablets ($p< 0.05$). The tablets also, exhibited percentage friability range between 0.9 to 1.4 %. Garlic tablets formulated with acacia significantly ($p< 0.05$) exhibited the fastest disintegration time across all batches. The order of tablets performance in terms of disintegration time is acacia > gelatin > SCMC. The phytochemical results of extracts of *Allium sativum* indicate the presence of alkaloids, saponin, flavonoids, carbohydrates and proteins. Therefore, garlic tablets could be formulated by wet granulation using acacia, gelatin or SCMC in order to standardize the formulation.

Keywords: *Allium sativum,* tablets, quality control, garlic, phytochemicals.

INTRODUCTION

Allium sativum L. (Liliaceae) commonly called garlic is one of the herbs most commonly used in modern folkloric medicine for the treatment of many ailments. Garlic was an important medicine to the ancient Egyptians listed in the medical text Codex Ebers (ca. 1550 BC)[1-3]. The therapeutic use of garlic has been recognized as a potential medicinal value for thousands of years. The antifungal, antiviral, antibacterial, anthelmintic, antiseptic and anti-inflammatory properties of garlic are well documented [4]. Moreover, garlic extracts exhibited activity against both gram negative (*E. coli*, *Salmonella* sp. and *Citrobacter enterobacter*, *Pseudomona kilabsella*) and gram positive (*S. aureus*, *S. pneumonia,* Group A *streptococcus* and *Bacillus anthrax*) all of which are cause of morbidity Worldwide[4]. The current medicinal uses are to prevent and treat cardiovascular disease by lowering blood pressure and cholesterol, as an antimicrobial, and as a preventive agent for cancer. Pooled data from numerous randomized trials suggest that garlic lowers total cholesterol concentrations by approximately 10% and favourably alters HDL/LDL ratios[5]. Garlic also inhibits platelet aggregation and enhances fibrinolytic activity, reducing clots on damaged endothelium. Epidemiologic data, *in vitro* studies and animal data suggest that garlic may help prevent some solid tumors[5]. Garlic has also been proposed for the treatment of asthma, candidiasis, colds and diabetes[6]. African herbalists use garlic to treat respiratory infections and helminthic infections; many African families use garlic oil drops to treat childhood ear infections[7]. Han et al.[8] reported that the antibiotic activity of 1mg of allicin, is equated to that of 15 IU of penicillin.

The active constituents are several complex sulfur-containing compounds that are rapidly absorbed, transformed and metabolized. Garlic contains a variety of effective compounds that exhibit anticoagulant (anti-thrombotic)[9-13], antioxidant,[14-15], antibiotic[16-18], hypocholesterolaemic[19], hypoglycaemia[20], as well as hypotensive activities [19]. As mentioned above, although a large number of sulphur-thiosulphinates are present in sufficient quantities at normal consumption levels (3-5 g per day). Allicin has been shown to be important in many health effects of garlic [21]. However, the anti-cancer effect of garlic might be shared between allicin and other unidentified compounds [22]. Garlic contains about 1% alliin, which is converted enzymatically by allicinase to allicin, and other sulphur-containing compounds [23]. Garlic has been given as a fresh juice, lyophilized powders and as steam distilled oil [24]. Garlic can be provided in the form of capsules and powders, as dietary supplements, and thus differ from conventional foods or food ingredients [25].

The primary benefit of using plant-derived medicine is that they are relatively safer than synthetic alternatives, offering profound therapeutic benefits and more affordable treatments [26]. In view of the widespread use of herbal products, important technical aspects such as standardization and quality control will be of immense benefit in order to enhance their efficacy and improve patients' compliance [27-29].

Tablets have remained the most common dosage form by which medicaments are usually administered to patients

because of their advantages over the other dosage forms[30] and account for 70 % - 80 % of all pharmaceutical dosage forms [31]. The aim of the work is to standardize *Allium sativum* by formulating them into tablets dosage form in order to encourage the use of this drug and also enhance patient compliance.

MATERIALS AND METHODS

Maize starch, acacia, gelatin (BDH, England), sodium carboxymethylcellulose and magnesium stearate (May and Baker, England), distilled water (Lion water, Nsukka, Nigeria), hydrochloric acid, lactose (Merck, Germany). Garlic powder was obtained from the dried bulb of *Allium sativum* processed in our laboratory. All other reagents and solvents were analytical grade and were used as supplied.

Preparation of garlic powder

Allium sativum bulbs were collected from Jos, Nigeria in the month of January, 2008. The plant material was authenticated by Mr. A.O. Ozioko, a consultant taxonomist with the International Center for Ethnomedicine and Drug Discovery (InterCEDD) Nsukka. The voucher specimen of the plant was deposited in the herbarium of the Department of Pharmacognosy and Environmental Medicines, University of Nigeria, Nsukka. The bulb and cloves were peeled, cut into chips and dried at room temperature for 63 days. Maize starch was added to the garlic chips at a ratio of 1:1 to adsorb the garlic oil and aid in the particle size reduction. The garlic chips were then milled using a grinder (Kenitone Millennium Quality, SO300B) and screened through size no 10 (1.7 mm) to obtain granules of uniform size which were further dried and also screened through sieve number 16 (size 1.0 mm) to further obtain uniform size granules.

Phytochemical screening

Phytochemical tests were carried out on garlic powdered extract for the presence of alkaloids, saponins, flavonoids, carbohydrates and proteins. The tests were carried out using standard procedures of analysis [32-33].

Preparation of garlic tablets

Three binders acacia, gelatin and SCMC were used at concentrations of 1, 2, 4 and 8 % w/w to prepare the granules as shown in Table 1. Garlic powder (10 % w/w), the disintegrant (5 % w/w), the tartrazine (colourant) and the diluents (lactose) were properly mixed in a tumbler mixer for 10 min. The powder mixtures were moistened with the appropriate amount of binder solution. The homogeneous wet mass was then screened through a 1.7 mm sieve and the wet granules dried in a hot air oven at 60°C for 1 h. Thereafter, the dried granules were screened through a 1.0 mm sieve (Jurgus and Co., Western Germany). The granules were mixed with magnesium stearate, and the tablets were prepared by compressing the lubricated granules at 46-48 kgf using a 9.0 mm punch and die set fitted into an automated F3 Manesty Single Punch tabletting machine (Manesty, England).

Table 1: Composition of *Allium sativum* tablets

Ingredient/tablet in mg				
Garlic powder	30.0	30.0	30.0	30.0
Binder*	3.0	6.0	12.0	24.0
Maize starch	15.0	15.0	15.0	15.0
Tartrazine	3.0	3.0	3.0	3.0
Magnesium stearate	3.0	3.0	3.0	3.0
Lactose qs	300.0	300.0	300.0	300.0

*Acacia, gelatin and SCMC

Uniformity of weight

To study the weight variation, 20 tablets from each batch were weighed individually using an electronic balance (Ohaus Adventurer, China) and the test was performed according to the official method [34].

Disintegration time test

Disintegration time test was conducted using an Erweka ZT4 basket and rack assembly (Erweka, Germany) and 0.1 N HCl maintained at 37.0 ± 1.0 °C as the disintegration medium. Ten tablets from each batch were used for the test and the procedure being as stipulated in the BP [34].

Crushing strength test

Crushing strengths of tablets were determined using Monsanto-Stokes hardness tester. All measurements were made in triplicates and the mean crushing strength recorded.

Tablet friability test

The test was performed using a Roach friabilator (Campbell Electronics, Mumbai, India). Twenty tablets were randomly selected from each batch of the tablet. The tablets were dedusted and weighed. The tablets were placed into the drum of the friabilator and rotated at 25 rpm for 4 min. The tablets were removed from the friabilator, dedusted and reweighed. The friability result was expressed as loss of mass expressed as a percentage of the initial mass [34]. The percentage friability was calculated from the equation below:

$$Friability\ (\%) = 100\left[\frac{W_o - W}{W_o}\right] \quad (1)$$

where W_o and W are the initial weight and final weight of the tablets respectively.

Statistical analysis

Data were analysed by one-way analysis of variance (ANOVA). Differences between means were assessed by a two-tailed student's T-test. $P < 0.05$ was considered statistically significant.

RESULTS AND DISCUSSION

Uniformity of weight

Tablet weight uniformity test is an important quality control test because variation in tablets weight will lead to variation in drug content which could also affect the overall bioavailability of the drug. The results of tablets weight uniformity test are shown in Table 2, from the values obtained, the tablets weight ranged from 301.20 ± 0.40 to 312.40 ± 2.11 mg. The percentage deviations obtained from the results showed that the garlic tablets formulated with different binders at varying concentrations significantly (p< 0.05) exhibited percentage deviation of < 5 % stipulated in official book for tablets weight ≥ 250 mg [34].

Table 2: Some properties of garlic tablets

Batch	Weight (mg ± CV)*	Hardness (kgf ± SD)[a]	Friability (%)*
A1 (2 % acacia)	303.00 ± 1.90	4.80 ± 0.15	1.20
A2 (4 % acacia)	309.20 ± 3.90	5.00 ± 0.17	1.10
A3 (6 % acacia)	311.00 ± 1.30	5.30 ± 0.13	1.00
A4 (8 % acacia)	312.40 ± 2.11	6.80 ± 0.13	1.00
B1 (2 % gelatin)	301.20 ± 0.40	3.10 ± 0.11	1.40
B2 (4 % gelatin)	303.00 ± 1.20	5.30 ± 0.07	1.20
B3 (6 % gelatin)	306.20 ± 2.80	5.50 ± 0.11	1.00
B4 (8 % gelatin)	307.20 ± 1.90	5.90 ± 0.23	1.00
C1 (2 % SCMC)	305.40 ± 3.00	4.90 ± 0.17	1.10
C2 (4 % SCMC)	302.80 ± 1.80	5.30 ± 0.12	1.10
C3 (6 % SCMC)	302.80 ± 1.10	5.80 ± 0.10	1.00
C4 (8 % SCMC)	307.40 ± 1.70	7.20 ± 0.19	0.90

*Mean for 20 tablets, [a]Mean for 10 tablets ± SD, CV: coefficient of variation, SD: standard deviation, A1, A2, A3 and A4 contain 2 , 4, 6 and 8 % w/w acacia, B1, B2, B3, and B4 contain 2, 4, 6, and 8 %w/w gelatin, C1, C2, C3 and C4 contain 2, 4, 6, and 8 %w/w SCMC; SCMC: sodium carboxymethylcellulose, P < 0.05 was considered significant.

Crushing strength

The results of the crushing strength test of garlic tablets are shown in Table 2. The results revealed that the tablets hardness ranged from 4.80 ± 0.15 to 6.80 ± 0.13 kgf for tablets formulated with acacia as binder, 3.10 ± 0.11 to 5.90 ± 0.23 kgf for tablets formulated with gelatin and 4.90 ± 0.17 to 7.20 ± 0.19 kgf for tablets formulated with SCMC. Therefore, the results showed that the crushing strength of the tablets was affected by the binder type and concentration used. Increase in binder concentration significantly caused an increase in the crushing strength of the tablets (p< 0.05). The results showed that all the tablets complied with BP specifications for hardness test of between 5 – 8 kgf [34]. However, batch B1 formulated with 2 % gelatin failed the crushing test. The order of tablets hardness in increasing order for the binders is: SCMC > acacia > gelatin.

Tablets friability

Friability test measures the ability of the tablets to withstand shock and vibrations during packaging, handling, transportation and use. The results of tablets friability test are presented in Table 2. The tablets exhibited percentage friability range between 0.9 to 1.4%. Values of friability between 0.8-1 % are often regarded as upper limit of acceptance [34]. The results therefore revealed that most of the formulations passed the friability tests. The friability results were also directly affected by the concentration of binder used in the formulation.

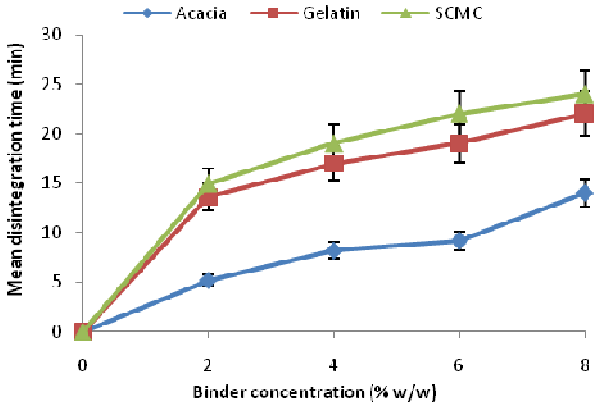

Figure 1: Effect of binder type and concentration on the disintegration time of garlic tablets

Disintegration time of tablets

The results of the disintegration time of tablets and the effect of binder type and concentration on the disintegration time of tablets are shown in Fig. 1. From the results, tablets formulated with acacia significantly (p< 0.05) exhibited the fastest disintegration time of all the batches and complied with BP [34] specifications for normal release tablets of ≤ 15 min. However, garlic tablets formulated with gelatin and SCMC had higher disintegration time, and concentrations above 2 % are recommended for sustained release tablet formulations. Therefore, the disintegration time of tablets was affected by the binder type and concentration. Increase in concentration of binder caused an increase in the disintegration time of tablets (p< 0.05). The order of tablets performance in terms of fastness of the disintegration time is acacia > gelatin > SCMC.

Table 3: Some phytochemical constituents of *Allium sativum*

Phytochemical constituent	Remark
Alkaloids	+
Saponins	+
Flavonoids	+
Carbohydrates	+
Protein	+

+ present

Phytochemical constituents

The results of some phytochemical constituents of *Allium sativum* are presented in Table 3, the results showed that *Allium sativum* contains alkaloids, saponin, flavonoids, carbohydrates and proteins.

CONCLUSION

Garlic tablets were successfully formulated by wet granulation using acacia, gelatin and SCMC as binders. The tablets generally exhibited good physicochemical properties. Garlic tablets has advantages over other forms of delivery systems for this drug which include: increase in aesthetic appeal and mouth feel which would enhance patient compliance, increase in shelf life and stability of this drug and ease of administration and use. However, further research in this field of study is highly required in order to effectively make this drug available for use in the market.

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