INTRODUCTION

Cryptolepis sanguinolenta is a thin-stemmed twining and scrambling shrub up to 8 m long, containing yellow-orange juice which becomes red upon drying. It is a member of the family Apocynaceae (subfamily: Periplocoideae). The plant is native to West Africa and is found in countries like Ghana, Nigeria, Cote d’Ivoire, Guinea, Guinea-Bissau, Mali, Senegal, Sierra Leone, Angola, Congo, Uganda, and Cameroon [4]. It is a medicinal plant used by some traditional herbalist in the treatment of fever, urinary, and upper respiratory tract infections [4]. The use of this plant as a medical therapy has increased as it has been proposed that the root and leaf extracts have hypotensive, antipyretic, anti-inflammatory, anti diarrhoeal, in vitro antibacterial and antimalarial effects [5]. It is commonly called nibima, Kadze, gangamo, or yellow-die root. It is called paran pupa in the Yoruba-speaking areas of Nigeria [1]. Studies have documented the antidiabetic potentials of Cryptolepis sanguinolenta [6-8]. Crude extracts of C. sanguinolenta and their fractions, as well as indigoquinoline alkaloids isolated from the plant, have been shown to have activity against Plasmodium falciparum both in vitro and in vivo [6-8]. In addition to studies indicating anti-plasmodial effect, extracts of C. sanguinolenta have been shown to have anti-microbial [9-10] and anti-inflammatory activities [6]. Extracts from various morphological parts of Cryptolepis sanguinolenta are widely used traditionally in folklore medicine in many parts of the world for the management, control, and treatment of diabetes mellitus. The hypoglycemic activity of Cryptolepis sanguinolenta is associated with its influence to reduce intestinal glucose absorption and transport [6].

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 [11]. In recent times, focus on plant research has increased all over the world and a lot of evidence has been collected to show immense potential of medicinal plants used in various traditional systems [12]. Plants may become the bases for the development of a new medicine or they may be used as phyto-medicine for the treatment of disease [12]. It is estimated that today, plant materials are present in, or have provided the models for 50 % Western drugs [13]. Plant derived drug serve as a prototype to develop more effective and less toxic medicine [13]. Plants with anti malarial, anthelmintic, antidiabetic and anti-inflammatory properties have been of immense ethnomedicinal use to mankind. 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 patient’s compliance [14].

Tablet dosage forms are the most popular and preferred drug delivery systems in terms of precision of unit dose, low cost, patient compliance, and good physical and chemical stability and account for 70 % - 80 % of all pharmaceutical dosage forms [15]. Tablets have remained the most common dosage form by which medications are usually administered to patients because of their advantages over the other dosage forms [16]. Therefore the objective of this work is to formulate the methanolic extract of Cryptolepis sanguinolenta into tablets and to study the effect of different binders and binder concentration on the in vitro properties of the tablets.

MATERIALS AND METHODS

Lactose (Merck, Germany), maize starch, sodium carboxymethyl cellulose, gelatin, ethanol (BDH, England), magnesium stearate (May and Baker, England), distilled water (Lion water, Nsukka, Nigeria). Cryptolepis sanguinolenta root extract was obtained from a batch processed in our laboratory. All other reagents and solvents were analytical grade and were used as supplied.

Collection and authentication of plant material

Cryptolepis sanguinolenta roots were collected from the Army Barrack’s field along Edem road Nsukka, Enugu State, Nigeria in the month of June, 2011. The plant material was authenticated by Mr. A.O. Orakpo, 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.

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Preparation of plant extract for phytochemical analysis

Cryptolepis sanguinolenta roots were washed thoroughly in water, chopped into tiny pieces then dried in an air-circulating oven in the laboratory at 35 – 40°C. The dried roots were milled several times in an equipment of hammer mill type. The powdered roots (210 g) were extracted by maceration with 95 % ethanol for 48 h. The extract was filtered and concentrated to dryness using a rotary evaporator attached to a vacuum pump to obtain the crude powder extract (10 g) which was stored at a temperature of 40°C until use.

Phytochemical Screening

Phytochemical tests were carried out on the powdered extract for the presence of alkaloids, tannins, saponins, flavonoids, resins, fats and oils, steroids, glycosides, terpenoids, acidic compounds, carbohydrates, reducing sugars and proteins. The tests were carried out using standard procedures of analysis [18-20].

Preparation of granules

Granules were prepared by wet granulation method using two different binders at concentrations of 2 %, 4 %, 6 % and 8 %w/w. Details of granulation are given in Table 1. Lactose was used as the filler and maize starch BP as disintegrant (10 % w/w) were dried and mixed for 10 min in a tumbler mixer with the crude extract of Cryptolepis sanguinolenta. 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 55°C for 1 h. Thereafter, the dried granules were screened through a 1.0 mm sieve.

Table 1: Composition of Cryptolepis sanguinolenta tablet

<table>
<thead>
<tr>
<th>Batch</th>
<th>C. sanguinolenta extract (mg)</th>
<th>Gelatin (mg)</th>
<th>SCMC (mg)</th>
<th>Maize starch (mg)</th>
<th>Magnesium stearate (mg)</th>
<th>Lactose qs (mg)</th>
</tr>
</thead>
<tbody>
<tr>
<td>F1</td>
<td>5.0</td>
<td>6.0</td>
<td>-</td>
<td>15.0</td>
<td>3.0</td>
<td>300.0</td>
</tr>
<tr>
<td>F2</td>
<td>5.0</td>
<td>12.0</td>
<td>-</td>
<td>15.0</td>
<td>3.0</td>
<td>300.0</td>
</tr>
<tr>
<td>G1</td>
<td>5.0</td>
<td>-</td>
<td>6.0</td>
<td>15.0</td>
<td>3.0</td>
<td>300.0</td>
</tr>
<tr>
<td>G2</td>
<td>5.0</td>
<td>-</td>
<td>12.0</td>
<td>15.0</td>
<td>3.0</td>
<td>300.0</td>
</tr>
<tr>
<td>G3</td>
<td>5.0</td>
<td>-</td>
<td>18.0</td>
<td>15.0</td>
<td>3.0</td>
<td>300.0</td>
</tr>
<tr>
<td>G4</td>
<td>5.0</td>
<td>-</td>
<td>24.0</td>
<td>15.0</td>
<td>3.0</td>
<td>300.0</td>
</tr>
</tbody>
</table>

Key: F1 and F2 contain 2 and 4 %w/w gelatin, G1 – G4 contain 2, 4, 6, and 8 %w/w SCMC, SCMC: sodium carboxymethyl cellulose.

Preparation of tablets

Initially granules were treated with lubricant i.e. magnesium stearate. 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.

EVALUATION OF TABLETS

Disintegration time test

Disintegration time test was conducted using an Erweka ZT 120 basket and rack assembly 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, 2009 for normal release tablets [21].

Uniformity of Weight

Twenty tablets were randomly selected from each batch. The tablets were weighed individually using an electronic balance (Ohaus Adventurer, China) and the individual weights recorded. The mean weight, standard deviation and percentage deviation were calculated [22].

Tablet friability test

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 (Erweka GmbH, Germany) 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 [21]. The abrasion resistance B was calculated from the equation below:

\[ B = 100\left(1 - \frac{W}{W_0}\right) \]

where \( W_0 \) and \( W \) are the initial weight and final weight of the tablets respectively.

Hardiness/Crushing Strength Test

This test was carried out using a Monsanto-stokes hardness tester. Ten tablets from each batch were randomly selected. Each tablet was placed between the jaws of the hardness tester and force was applied by adjusting the knob of tester until the tablet integrity failed. The results were recorded in kgf.

Statistical analysis

Statistical analysis was carried out using SPSS version 14.0 (SPSS Inc. Chicago, IL.USA). All values are expressed as mean ± SD. 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

Phytochemical constituents of C. sanguinolenta root extract

Results of phytochemical screening of Cryptolepis sanguinolenta root extract are shown in Table 2. The results indicated the presence of very important phytochemicals. Phytochemical analysis of Cryptolepis sanguinolenta root revealed the presence of alkaloids, terpenoids, steroids, proteins, carbohydrate, resins, reducing sugars and glycosides in substantial quantities. Tannins, saponins, flavonoids and acidic compounds were however, not found in the plant root.

TABLET PROPERTIES

Weight uniformity

The results of tablets weight uniformity test presented in Table 3 showed that weights of C. sanguinolenta tablets ranged from 310.95 ± 2.42 to 311.15 ± 1.76 mg for batches F1 and F2 formulated with 2 and 4 % gelatin, 294.55 ± 1.65 to 303.90 ± 2.60 mg for tablets G1 and G2 formulated with 2 and 4 % SCMC. The low coefficient of variation exhibited by these formulations confirmed the reproducibility of these formulations and the reliability of the production process.

Disintegration time
The results of the disintegration time of C. sanguinolenta tablets are shown in Table 3. From the results, the tablets exhibited disintegration time range of 8.00 ± 0.10 to 31.00 ± 0.27 min for tablets formulated with 2 and 8 % SCMC (G1 and G4).

Tablets hardness

The results of tablets hardness are shown in Table 3. From the results, C. sanguinolenta tablets exhibited hardness that ranged from 4.76 ± 0.05 to 5.80 ± 0.07 kgf for F1 and F2 tablets formulated with 2 and 4 % gelatin and 2.00 ± 0.03 to 5.00 ± 0.07 kgf for tablets formulated with 2 and 8 % SCMC (G1 and G4). Generally, tablets formulated with gelatin showed higher hardness values than SCMC. The hardness of the tablet formulations was significantly affected by the concentration of the binder as shown in Table 3. From the results, tablets formulated with 2, 4, and 6 % SCMC (G1, G2 and G3) failed the tablets hardness test as shown in Table 3. However, tablets formulated with 2 and 4 % gelatin (F1 and F2) complied with BP specifications for tablets hardness with values of ≥ 5 kgf. The presence of alkaloids in high concentration in the plant root explains the traditional use of the plant for the treatment of malaria. The properties of the tablets were affected by the binder type and granulation method using gelatin and SCMC respectively as binders. Tablets friability results presented in Table 3 showed that tablets friability ranged from 0.84 to 1.28 % for F1 and F2 tablets formulated with 2 and 4 % gelatin and 0.92 to 1.31 % for tablets formulated with 8 and 4 % SCMC (G4 and G2). Friability test measures the resistance of the tablets to abrasion.

DISCUSSIONS

Phytochemical constituents of C. sanguinolenta root extract

The presence of alkaloids in high concentration in the plant root explains the traditional use of the plant for the treatment of malaria. The medicinal plants that are moderately rich in alkaloids have potential health promoting effects [22]. Crude extracts of C. sanguinolenta and their fractions, as well as indouquinoline alkaloids isolated from the plant, have been shown to have activity against Plasmodium falciparum both in vitro and in vivo as earlier reported [6-8]. The root of the plant also contains glycosides. Cardiac glycosides treat heart problems that may result from severe malaria attack. Phytochemicals are non-nutritive plant chemicals that have protective or disease preventive properties. Plants produce these chemicals substances to protect themselves, and they also protect humans against certain diseases [23].

Table 2: Phytochemical constituents of C. sanguinolenta roots extract

<table>
<thead>
<tr>
<th>Phytochemical constituents</th>
<th>Remarks</th>
</tr>
</thead>
<tbody>
<tr>
<td>Alkaloids</td>
<td>+++</td>
</tr>
<tr>
<td>Carbohydrates</td>
<td>++</td>
</tr>
<tr>
<td>Saponins</td>
<td>-</td>
</tr>
<tr>
<td>Reducing sugars</td>
<td>+++</td>
</tr>
<tr>
<td>Steroids</td>
<td>+++</td>
</tr>
<tr>
<td>Tannins</td>
<td>-</td>
</tr>
<tr>
<td>Glycosides</td>
<td>+++</td>
</tr>
<tr>
<td>Proteins</td>
<td>+++</td>
</tr>
<tr>
<td>Flavonoids</td>
<td>-</td>
</tr>
<tr>
<td>Resins</td>
<td>+++</td>
</tr>
<tr>
<td>Fats and oils</td>
<td>-</td>
</tr>
<tr>
<td>Acid compounds</td>
<td>-</td>
</tr>
<tr>
<td>Terpenoids</td>
<td>+++</td>
</tr>
</tbody>
</table>

Key: +++ High concentration, ++ moderate concentration, - absent

Table 3: Properties of C. sanguinolenta root extract tablets.

<table>
<thead>
<tr>
<th>Batch</th>
<th>Weight (mg ± CV)*</th>
<th>Hardness (kgf ± SD)*</th>
<th>Disintegration time (min ± SD)*</th>
<th>Friability (%)*</th>
</tr>
</thead>
<tbody>
<tr>
<td>F1 (2 % gelatin)</td>
<td>31.11 ± 1.76</td>
<td>4.76 ± 0.05</td>
<td>8.00 ± 0.10</td>
<td>1.28</td>
</tr>
<tr>
<td>F2 (4 % gelatin)</td>
<td>31.09 ± 2.42</td>
<td>5.80 ± 0.07</td>
<td>13.50 ± 0.21</td>
<td>0.84</td>
</tr>
<tr>
<td>G1 (2 % SCMC)</td>
<td>30.39 ± 2.60</td>
<td>2.00 ± 0.03</td>
<td>10.00 ± 0.17</td>
<td>1.07</td>
</tr>
<tr>
<td>G2 (4 % SCMC)</td>
<td>29.45 ± 1.65</td>
<td>3.06 ± 0.03</td>
<td>18.60 ± 0.11</td>
<td>1.31</td>
</tr>
<tr>
<td>G3 (6 % SCMC)</td>
<td>29.63 ± 1.31</td>
<td>4.18 ± 0.10</td>
<td>20.10 ± 0.23</td>
<td>1.04</td>
</tr>
<tr>
<td>G4 (8 % SCMC)</td>
<td>29.60 ± 1.78</td>
<td>5.00 ± 0.07</td>
<td>31.00 ± 0.27</td>
<td>0.92</td>
</tr>
</tbody>
</table>

*Mean for 20 tablets, -Mean for 10 tablets ± SD, CV: coefficient of variation, SD: standard deviation, F1 and F2 contain 2 and 4 %w/w gelatin, G1 – G4 contain 2, 4, 6, and 8 %w/w SCMC; SCMC: sodium carboxymethyl cellulose, P < 0.05 was considered significant.

CONCLUSION

Cryptolepis sanguinolenta root extract tablets were produced by wet granulation method using gelatin and SCMC respectively as binders. The properties of the tablets were affected by the binder type and concentration of the binder used in formulating the tablets. Increase in binder concentration caused an increase in hardness and disintegration time of tablets. The results obtained from the study showed that gelatin showed good properties for formulating Cryptolepis sanguinolenta normal release tablets than SCMC.

CONFLICT OF INTEREST

The authors state no conflict of interest.

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