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# Physico-Technical Properties of Tablets Formulated with Ethanolic Extract of Fresh Leaves of *Combretum Micranthum* G. Don

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**ABSTRACT**

This study is a follow-up to our recent study published elsewhere. It is aimed at determining the physico – technical and antibacterial profiles of tablets formulated using ethanolic extracts of *Combretum micranthum*, and also determine if they meet pharmacopoeial specifications. The fresh leaves of *Combretum micranthum* were harvested during the rainy season in Akwa Ibom State, Nigeria. They were thoroughly washed and rinsed with distilled water, divided into three portions, and dried in hot air oven at 48 ºC (Sample A), sun (Sample B) and at room temperature (Sample C). They were pulverized, macerated in a transparent extraction tank using 70 % ethanol for 72 h at room temperature, and concentrated. The activity of each extract was tested on typed cultures of *Staphylococcus aureus* (ATCC 6538) and *Escherichia coli* (ATCC 25922). The extract with the highest activity (Sample B) was selected for further studies. Phytochemical screening was carried out using standard methods. Six batches of granulations for tablets were produced using a predetermined formula. The flow rate, angle of repose, and compressibility indices of the granules were determined, and uniformity of weight, hardness, friability and disintegration time of the tablets were determined using pharmacopoeial methods. The results show that the sun-dried leaves of *C. micranthum* have constituents that exhibited the highest activity against cultures of *S. aureus* and *E. coli.* The phytochemical screening on the sun-dried leaves extract revealed that tannins were present in large quantities while phlobatannins and anthraquinones were absent. The results of the flow and compressibility properties of the granules from sun-dried extract revealed generally poor flow and high compressibility for all the batches. The tablet hardness values for all the batches were greater than 5 kg. The friability value for each batch was less than 1 %. The tablets have maximum disintegration time of 101 min. These results showed that the extract could be used to produce sustained release or delayed release tablets.

## INTRODUCTION

Infectious diseases caused by bacteria, viruses, fungi and other parasites are major causes of death in human in spite of the enormous progress recorded by the modern medicine (Batawila *et al*, 2005). The WHO (2002) and UNAIDS (2007) reported that between 14 and 17 million people die each year due to infectious diseases. In developing countries, infectious disease cause 43% mortality as against 1% in developed countries. The use of plant as source of remedies for the treatment of many infectious diseases dates back to prehistory, and people of all continents have this old tradition. Despite the remarkable progress in synthetic organic chemistry of the twenty-first century, over 25% of prescribed medicines in industrialized countries derive directly or indirectly from plants (Newman *et al*, 2000). However, many plants used in traditional medicine are still under studied, particularly in clinical microbiology (Kirby, 1996). In developing countries where medicines are quite expensive, investigation on antimicrobial activities of plants may still be needed. It is expected that many of the phytochemicals will find their way in the arsenal of anti-microbial drugs prescribed by physicians in pharmaceutical dosage forms e.g. compressed tablets, for oral administration with its physical and chemical integrity protected up to the point of ingestion (Cowan, 1999). Compressed tablets are oral solid dosage forms containing active substances (with or without suitable diluents) having their own identity while being free of defects such

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as chips, cracks, contamination, with good strength to withstand the rigor of mechanical shocks encountered during production, packaging, shipping and dispensing processes (Ofoefule, 2006). *Combretum micranthum* G. Don is a bushy shrub or creeper that may grow up to 20 m in length. The leaves are opposite, ovate and acuminate; the flowers are borne as auxiliary cluster on scaly stalks; the fruits are small with scaly and four winged. The medicinal value of the plant is due to the presence of certain substances such as amino acids, phenanthrenes and dihydrophenanthrenes, gums and glycosides (Osonwa *et al*, 2012). The present study is aimed at investigating the antibacterial and physico-technical properties of tablets formulated using ethanolic extracts of *Combretum micranthum* G. Don.

## MATERIALS AND METHODS

Fresh leaves of *Combretum micranthum*, ethanol (BDH, England), nutrient agar (Oxion, Hampshire, England), typed cultures of *Staphylococcus aureus* (ATCC 6538) and *Escherichia coli* (ATCC 25922). All other reagents used were of analytical grade.

### Collection and Identification of Plant

The fresh leaves *of Combretum micranthum* was collected on August 16th, 2010 from a farm land at Ikot Edebe, Nsit Atai LGA in Akwa Ibom State, Nigeria. The leaves were identified in the Herbarium Unit of the Department of Pharmacognosy and Natural Medicine, Faculty of Pharmacy, University of Uyo, Akwaibom State, Nigeria.

### Processing and extraction of the collected leaves

The leaves were thoroughly washed and rinsed with distilled water and were divided into three. The first portion was dried in the hot air oven at 48 ºC. The second portion was sun-dried. The third part was dried at room temperature. The different portions were pulverized, and macerated in a transparent extraction tank using ethanol for 72 h at room temperature. There was intermittent stirring to allow for a good mix. The mixture was then filtered using glass funnel fitted with cotton wool. The filtrate collected in a beaker was subsequently concentrated to dryness in a water bath at 40 ºC to obtain a dark gummy extract. The extract was weighed and the percentage yield in each case was calculated (Fyhrquist *et al*, 2002). The extracts were labeled A - oven-dried; B - sun-dried, and C - room temperature-dried.

### Yield of the extract

The percentage yield of the extract was obtained after extraction of the different portions of the leaves using equation 1:

$$\text{Percentage Yield (\%)} = \frac{W_a}{W_b} \times 100 \ \% \quad \text{.....(1)}$$

Where $W_a$ = Weight of the extract; $W_b$ = Weight of the extracted leaves.

### Phytochemical screening

Phytochemical screening to determine the presence of alkaloids, tannins, saponins and anthraquinones, cardiac glycosides, flavonoids were performed on the extracts using standard chemical tests prescribed by Sofowora (Sofowora, 1993).

### Antibacterial screening and determination of minimum inhibitory concentration (MIC)

This was performed using Agar-well diffusion method. Sterile Petri dishes were aseptically inoculated with 0.1 ml of suspension of the test organism and 20 ml of the culture media (molten agar). The mixture was swirled gently to mix and allowed to solidify. Using a sterile flamed cork-borer, holes were bored on the seeded agar plates, discarding the removed agar rings into the disinfectant solution; the wells were aseptically filled with the different dilutions of the extract using Pasteur pipette as follows: 0.25, 0.5, 1, 2, 5, 10, 20, 30, 40, 60, 80 and 100 mg/ml of each extract. The plates were allowed to stay for 30 min on the bench before incubation to allow for diffusion of the agents into the media before the growth of the microorganism (Ordonez *et al*, 2003). The plates were incubated at 37 ºC for 24 h for bacteria. The plates were observed and diameters of the inhibition zones were measured. The plot of log concentration against inhibition zones was performed to extrapolate the minimum inhibitory concentration (MIC). The extract with the highest activity (sun-dried extract) was selected for further studies (Shargel *et al*, 2004).

**Table. 1:** Formula for production of tablet batches. Total tablet weight = 500 mg.

| Batch | Drug (%) | MCC (%) | Starch (%) | Mg Stearate (%) |
|---|---|---|---|---|
| A | 40(200 mg) | 60.00 | - | - |
| B | 40(200 mg) | 55.00 | 5 | - |
| C | 40(200 mg) | 54.75 | 5 | 0.25 |
| D | 40(200 mg) | 54.50 | 5 | 0.5 |
| E | 40(200 mg) | 49.75 | 10 | 0.25 |
| F | 40(200 mg) | 49.50 | 10 | 0.5 |

**Table. 2:** Quantity of Component in each Batch for 40 Tablets

| Batch | Extract 'B' (g) | Avicel®(MCC) (g) | Maize Starch (g) | Mg Stearate (g) |
|---|---|---|---|---|
| A | 8.0 | 12.00 | | |
| B | 8.0 | 11.00 | 1.0 | |
| C | 8.0 | 10.95 | 1.0 | 0.5 |
| D | 8.0 | 10.90 | 1.0 | 0.1 |
| E | 8.0 | 9.95 | 2.0 | 0.05 |
| F | 8.0 | 9.90 | 2.0 | 0.1 |
| TOTAL | 48.0 | 64.7 | 7.0 | 0.3 |

### Granule preparation

Using the most potent extract (sun-dried), six batches of granules for tablets were produced to give 40 tablets per batch. The tablets were formulated by direct compression. The following excipients were employed: microcrystalline cellulose (MCC) (Avicel® PH 101®), maize starch and magnesium stearate as lubricant. The granules were produced by simple bulk mixing. The formula for each batch, percentage composition and weight of ingredients for each batch is as shown in tables 1 and 2.

**Granule Compressibility and Flow ability**

The compressibility parameter was determined using a 100 ml measuring cylinder. The granules were gently poured into the cylinder and the bulk volume, Vb was read off; the cylinder was then tapped until the granules assumed a constant of volume, Vt.

The bulk density, Dt was calculated as

$$Dt = \text{mass of granules (g)} / Vb \quad (2)$$

Tapped density, Dt was calculated as

$$Dt = \text{mass of granules (g)} / Vt \quad (3)$$

Carr's compressibility index was calculated as

$$(Dt-Db)/Dt \times 100\%. \quad (4)$$

**Tablet compression**

Since the granules had poor flow properties, they were manually fed into the die cavity of the single punch tableting machine using a spatula, and then compressed. The quantity of granules fed into the die was 500 mg in each case, carefully weighed out using an analytical balance.

**Characterization of tablet**

***Hardness Test***

The hardness test was carried out using a Monsanto Tablet Hardness tester to measure the force required to break a tablet when the force generated by a coiled spring is applied diametrically. The force was measured in kilogram force (kgF). 20 tablets per batch were used for this determination, and the mean hardness was calculated using the equation:

$$\text{Mean hardness} = \sum \frac{H_n}{n} \quad .....(5)$$

Where $\sum H_n$ = Sum of hardness value for tablets up to 20; n = total number of tablets

***Friability Test***

The Friability tests were conducted with a Roche friabilator, using 20 tablets for each batch at 25 rpm. The tablets were dedusted, weighed together and friabilated. The friabilated tablets were re-weighed, and calculated using the equation:

$$\text{Friability} = \frac{W_0 - W_1}{W_0} \times 100\ \% \quad .....(6)$$

Where: $W_0$ = Weight of 20 tablets, $W_1$ = Weight of tablets after friabilation.

***Weight Uniformity Test***

This test was done using an electronic weighing balance to weigh 20 tablets picked randomly from each batch individually. Then, the average weight, percentage deviation and standard deviations were calculated for each tablet batch.

***Disintegration Time Test***

Disintegration time test was performed using a USP XXIII Disintegration Apparatus. Six tablets were tested at the same time. The dissolution medium was 500 ml of distilled water.

**RESULT AND DISCUSSION**

**Yield of extract**

After extraction, the percentage yields of the various portions of the leaves obtained were as given in table 3. A dark gummy extract was obtained in each case. The highest percentage yield of 12.4% was obtained with the sun-dried leaves while the least was the oven-dried. The amount of phytoconstituents obtained in each case could be as a result of the use of a polar solvent (ethanol) which will extract only polar constituents. In addition, the low yield from oven-dried leaves could be due to the degradation effects of heat on the secondary metabolites at 48 ºC.

**Table. 3:** Percentage yield of extract.

| Leaves | Weight of powders (g) | Weight of extract (g) | Yield (%) | Appearance |
|---|---|---|---|---|
| Oven-dried | 204 | 11 | 5.4 | Dark, gummy |
| Sun-dried | 450.7 | 55.75 | 12.4 | Dark, gummy |
| Room-dried | 153 | 15 | 9.8 | Dark, gummy |

**Antibacterial screening and determination of Minimum Inhibitory Concentration (MIC)**

The result of the antibacterial screening and the determined MICs are shown in tables 4 and 5. From the results, the order of inhibition of growth of *S. aureus* is: extract B ($IZD_{max}$ = 22 mm at 100 mg/ml)> extract A ($IZD_{max}$ = 20 mm at 100 mg/ml)> extract C ($IZD_{max}$ = 18 mm at 100 mg/ml). Interestingly, only extract B inhibited the growth of the test *E. coli* with an $IZD_{max}$ of 16 mm at 100 mg/ml while extracts A and C showed no activity against the organism. This is in agreement with our recent report on *C. micranthum* (Osonwa *et al*, 2012).

Tannins were the major phytochemicals present in the extracts, and the antimicrobial properties of tannins have being reported (Chung et al, 1998a; Chung et al, 1998b; Rauha et al, 2000). Tannin is a polyphenol and has being reported to have microbicide activities against both gram positive and gram negative bacteria (Scalbert, 1991). The possible mechanism of their action might be inhibition of the hydrolytic enzymes (proteases and carbohydrases) of bacteria or other interactions to inactivate microbial adhesions and cell envelope transport proteins (Cowan, 1999; Karou *et al*, 2005).

Likewise, the MICs of the extracts for *S. aureus* are in the order: extract B>extract A>extract C. A very low MIC corresponds to a very strong antibacterial activity while a high MIC means a weak antibacterial activity. This confirms that the extract B has the strongest antibacterial activity while the extract C has the weakest antibacterial activity for *S. aureus*. The MIC of extract B for *E. coli* does not mean that the extract is weak against the test organism because it was the only extract that showed activity against the test organism.

**Phytochemical screening**

The phytochemicals present in the leaves are presented in table 6. The results of the phytochemical screening show that saponins, flavonoids, cardiac glycosides and terpenoids are present

**Table. 4:** Results of antibacterial efficacy of each extract.

| Concentration of extract (mg/ml) | *S. aureus* ATCC 6538 Mean IZD ± SD (mm) | | | *E. coli* ATCC 25922 Mean IZD ± SD (mm) | | |
|---|---|---|---|---|---|---|
| | A | B | C | A | B | C |
| 100 | 20 ± 1.2 | 22 ± 1.5 | 18 ± 1.3 | - | 16 ± 1.4 | - |
| 80 | 17 ± 1.0 | 21 ± 1.5 | 16 ± 1.1 | - | 14 ± 1.2 | - |
| 60 | 17 ± 1.2 | 21 ± 1.0 | 16 ± 1.3 | - | 14 ± 1.2 | - |
| 40 | 16 ± 1.2 | 17 ± 1.1 | 14 ± 1.1 | - | 14 ± 1.2 | - |
| 30 | 18 ± 1.5 | 20 ± 1.3 | 18 ± 1.3 | - | - | - |
| 20 | 18 ± 1.0 | 18 ± 1.2 | 18 ± 1.4 | - | - | - |
| 10 | 16 ± 0.9 | 18 ± 1.1 | 16 ± 1.2 | - | - | - |
| 5 | 16 ± 0.5 | 18 ± 1.0 | 14 ± 1.2 | - | - | - |
| 2 | 12 ± 1.1 | 16 ± 1.3 | 8 ± 0.9 | - | - | - |
| 1 | 8 ± 1.0 | 12 ± 1.2 | 6 ± 0.5 | - | - | - |
| 0.5 | - | - | - | - | - | - |
| 0.25 | - | - | - | - | - | - |

IZD – Inhibition Zone Diameter

**Table. 5:** MIC of each extract.

| Extract | Minimum Inhibitory Concentration (MIC) (mg/ml) | |
|---|---|---|
| | *S. aureus* ATCC 6538 | *E. coli* ATCC 25922 |
| A | 0.063 | - |
| B | 0.0036 | 2.24 |
| C | 0.14 | - |

**Table. 6:** Result of phytochemical screening of the extracts of *Combretum micranthum* G. Don.

| Phytochemical | Abundance | Remarks |
|---|---|---|
| Alkaloids | - | Absent |
| Saponins | + | Present in trace amount |
| Tannins | +++ | Present in abundance |
| Phlobatanins | - | Absent |
| Anthraquinones | - | Absent |
| Flavonoids | + | Present in trace amount |
| Cardiac glycosides | + | Present in trace amount |
| Terpenoids | + | Present in trace amount |

**Table. 7:** Results of the compressibility and flow tests results of the granules.

| Batch | Bulk density (g/cm$^3$) | Tapped density (g/cm$^3$) | Hausner's ratio | Carr's index (%) | Remarks |
|---|---|---|---|---|---|
| A | 0.49 | 0.63 | 1.29 | 25 | Poor flow |
| B | 0.49 | 0.67 | 1.37 | 30 | Poor flow |
| C | 0.49 | 0.67 | 1.37 | 27 | Poor flow |
| D | 0.49 | 0.66 | 1.35 | 26 | Poor flow |
| E | 0.49 | 0.72 | 1.47 | 32 | Poor flow |
| F | 0.49 | 0.73 | 1.52 | 34 | Poor flow |

*A = 200 mg drug + MCC; B = 200 mg drug + MCC + 5 % starch; C = 200 mg drug + MCC + 5% starch + 0.25% Mag. St.; D = 200 mg drug + MCC + 5% starch + 0.5% Mag. St.; E = 200 mg drug + MCC + 10 % starch + 0.25 % Mag. St.; F = 200 mg drug + MCC + 10 % starch + 0.5 % Mag. St.*

**Table. 8:** Tablet Properties.

| Batch | Mean weight ± SD (g) | Mean Hardness ± SD (KgF) | Friability (%) | Disintegration time (min) |
|---|---|---|---|---|
| A | 0.484 ± 0.0002 | 7.3 ± 0.3 | 0.42 | 101.00 |
| B | 0.487 ± 0.0003 | 10.4 ± 1.2 | 0.13 | 92.08 |
| C | 0.471 ± 0.0002 | 7. 5 ± 0.2 | 0.26 | 80.35 |
| D | 0.516 ± 0.0002 | 10.0 ± 0.8 | 0.16 | 94.55 |
| E | 0.472 ± 0.0001 | 5.0 ± 0.2 | 0.38 | 35.35 |
| F | 0.505 ± 0.0002 | 8.0 ± 1.6 | 0.26 | 36.40 |

in trace amounts. Alkaloids, phlobatanins and anthraquinones are absent while tannins are present in abundance. This is in agreement with previous report (Baba-Mousa *et al*, 1999; Simon *et al*, 2003; Batawila *et al*, 2005). There is the possibility that the antibacterial activity of the extract of this plant might be attributed to the presence of the tannins alone or in combination with the other compounds. However, it has being reported that the content of secondary metabolite in the plant is related to the nature of the soil and microclimate to which it is exposed (Coulidiati *et al*, 2009).

**Compressibility and Flow tests of the granules**

The granule compressibility properties (Carr's indices) are shown in Table 7. The values show that all the batches of the granules have poor flow properties. Batch A had the lowest Carr's index and Hausner's ratio of 25 % and 1.29 respectively, and batch F had the highest Carr's Index and Hausner's ratio 34% and 1.52 respectively. Introduction of a lubricant (magnesium stearate) brought down the Carr's indices (27 and 26 %) for batches C and D respectively, though it did not give the batches good flowability. The poor flow observed with the granules might be due to the high

interparticulate forces such as non-specific van der Waals forces or surface tension between adsorbed liquid layers at the particles surfaces, leading to increased adhesion and cohesion between the particles of the granules. This high friction between particles might be an indication of increased concentration of fines than free-flowing granules.

**Tablet characterization**

From the table 8, all the tablet batches had uniform tablet weight. This is because there was no significant difference between tablet weights. This shows that the adapted method of tablet formulation (direct compression) was good. It might also be due to the proper mixing of the formulation ingredients.

The hardness test results show that all the batches had good hardness profile (>5 kgF). The hardness results were in the order: B > D > F > C > A > E. Thus, batch E (drug 200 mg + MCC + 10 % starch + 2.5 % lubricant) had the lowest hardness of 5.0 ± 0.2 KgF while Batch B (drug 200 mg + MCC + 5 % starch) had the highest hardness (10.4 ± 1.2 KgF) hardness value. The reduction in hardness value might be due to the low concentration of binder added to the tablet batch E. Tablet tensile strength (hardness) can be used to predict comparative tablet bond strength, capping and lamination tendencies. The provision of the cohesiveness required for the compaction of solid particles to form tablets is the major role of a binder. From the result of the friability test, no batch exceeded the pharmacopoeial friability limit of 1 %. The friability ranges were in the order: B<D<F<C<E<A. Thus, batch B (drug 200 mg + MCC + 5 % starch) had the lowest friability of 0.13 % while Batch A (drug 200 mg + MCC) had the highest friability of 0.42 %. The good friability profile of the tablet batches might be due to the binder concentrations used or the quantity of wetting agent used for binder preparation before incorporation. From the result of the disintegration test, the disintegration times are in the order: A>D>B>C>F>E. Batch E ( drug 200 mg + MCC + 10 % starch + 0.25 % magnesium stearate) showed the lowest disintegration time of 35.35 min and batch A (drug + MCC) showing the highest disintegration time of 101.00 min. Batch A had no disintegrant (starch). These results show that the extract produces tablets that take a long time to disintegrate. Thus, the extract could be used to formulate delayed or sustained release tablets.

## CONCLUSION

The ethanolic extract of the sun-dried leaves of *Combretum micranthum* has significant activity against *S. aureus* and to a lesser extent on *E. coli.* Activity is higher when the leaves are sun-dried, than when oven-dried or dried in the shade. Granules produced from the extract with microcrystalline cellulose, maize starch and magnesium stearate have poor flow, but high compressibility. The tablets produced from the granules have good hardness, good friability property and prolonged disintegration time. Hence, sun-dried extracts of *C. micranthum* should be used to produce granules which could be used to formulate tablets with sustained or delayed release action.

## REFERENCES

*AIDS Epidemic Update* [Online]; UNAIDS-World Health Organization, 2007. http://data.unaids.org/pub/EPISlides/2007/2007epiupdate_en.pdf. (Accessed July 12, 2012)

Baba-Moussa F., Akpagana K., Bouchet P. Antifungal activities of seven West African *Combretaceae* used in Traditional medicine. J. Ethnopharmacol. 1999; 66: 335-338

Batawila K., Kokou K., Koumaglo K., Gbeassor MA., de Foucault B., Bouchet P., Akpangana K. Antifungal activity of five *Combretaceae* used in Togolese traditional Medicine. Fitoterapia. 2005; 76:264-268.

Chung KT., Lu Z., Chou MW. Mechanism of inhibition of tannic acid and related compounds on the growth of intestinal bacteria. Food Chem. Toxicol. 1998a; 36: 1053-1060

Chung KT., Wong TY., Wei CI., Huang YW., Lin Y. Tannins and human health: A Review. Crit. Rev. Food Sci. Nutr. 1998b; 38(6): 421-464

Coulidiati TH., Millogo-Kone H., Lamien-Meda A., Lamien CE., Lompo M., Kiendrebeogo M. Antioxidant and antibacterial activities of *Combretum nioroense* Aubrev. Ex. Keay (*Combretaceae*). Pak. J. Biol. Sci. 2009; 12 (3): 264-269

Cowan MM. Plants products as antimicrobial agents. Clin. Microbiol. Rev. 1999; 12:564-582

Fyhrquist P., Mwasumbi L., Haeggstrom CA., Vuorela H., Hiltunen R., Vuorela P. Ethnobotanical and antimicrobial investigation on some species of *Terminalia* and *Combretum* (Combretaceae) growing in Tanzania. J. Ethnopharmacol. 2002; 79: 169-177

Karou D., Dicko HMJ., Simpore J., Traore AS. Antioxidant and Antibacterial activities of Polyphenols from ethnomedicinal plants of Burkina Faso. *Afri. J. Biotechnol.* 2005; 4(8):823-828.

Kirby GC. Medicinal plants and the control of parasites. Trans. Roy. Soc. Trop. Med. Hyg. 1996; 90: 605-609

Newman DJ., Cragg GM., Snader KM. The influence of natural products upon drug delivery. Nat. Prod. Rep. 2000; 17:175-285

Ofoefule SI. A text book of Pharmaceutical Technology and Industrial Pharmacy. Samakin (Nig) Enterprises, Lagos, (2006) 49-59, 60.

Ordonez AA., Cudmani NM., Gomez D., Vattuone MA., Isla MI. Antimicrobial activity of nine Extracts of *Sechium edule* (Jacq) Swartz. Microb. Eco. Health Dis. 2003; 15:33-39.

Osonwa UE., Umeyor CE., Uduak VO., Uronnachi EM., Nwakile CD. Stability studies on the aqueous extract of the fresh leaves of *Combretum micranthum* G. Don Used as antibacterial agent. J. Chem. Chem. Eng. 2012; 6: 417-424

Rauha JP., Remes S., Heinonen M. Antimicrobial effects of Finnish plant extracts containing flavonoids and other phenolic compounds. Int. J. Food Microbiol. 2000; 56: 3-12

Scalbert A. Antimicrobial properties of tannins. Phytochemistry. 1991; 30: 3875 – 388

Shargel L., Mutrick AH., Souney PF., Swanson LN. Comprehensive Pharmacy review. 5th ed. Lippincott William and Wilkins, Philadelphia (2004) 64, 65, 519.

Simon G., Dewelle J., Nacoulma O., Guissou P., Kiss R., Daloze D., Brackman JC. Cytotoxic pentacyclic triterpenes from *Combretum nigricans*. Fitoterapia. 2003; 74: 339-344

Sofowora A. Medicinal Plants and traditional medicine in Africa. 2nd ed. Spectrum Books Ltd, Ibadan (1993) 150-156.

*WHO Global Burden of Diseases (GBD) estimates* [Online]; The World Health Organization, 2002. http://www.who.int/healthinfo/bodestimictes/en/ (Accessed on July 12, 2012).

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