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**Herbal medicines used in the treatment of typhoid in the Ga East Municipality of
Ghana**

Abstract

In Ghana, majority of the people patronize herbal medicines for the treatment of both chronic and acute ailments as well as infectious and noninfectious diseases. As such, the use of herbs as medicines in the treatment of enteric (typhoid) fever is very widespread.

Aims: This study therefore investigates anti-typhoidal herbal medicinal formulations for sale on the Ghanaian market with regards to the contents on the product labels and assesses the various active plant components in the light of documented evidence of their use in the treatment of typhoid.

Methodology: Herbal products for the treatment of typhoid were sampled from herbal medicine shops and pharmacies and assessed for the type of formulation, plant and non-plant constituents, dosage, indications, treatment duration and contraindications.

Results: Majority of the products (87%, n=16) had registration numbers whilst 13% had none. These anti-typhoid formulations were simultaneously recommended for the treatment of malaria (56%) (9 out of 16 products), jaundice (31%), various types of pains (body pains, headache, menstrual pains) (8%), stress (8%) and fatigue (8%). All the preparations had more than one plant as its active constituent. Forty four percent (44%) contained 2 plants species as the active ingredients, 37% contained between 3 to 5 plant species, 13% contained 6 to 10 plant species and 6% contained more than 10 plant species. The most frequently occurring active plant constituents of these products were *Carica papaya* L. (Caricaceae), *Morinda lucida*. (Rubiaceae), *Citrus aurantifolia* (Rutaceae), *Vernonia amygdalina* (Compositae) and *Azadirachta indica* (Meliaceae).

Conclusion: In all, thirty five different plant species belonging to 25 families were found to be present in these products. A literature search on the plants species showed that their

28 traditional use in the treatment of typhoid is well documented and hence their resulting
29 formulations may as well be very effective.

30 **Keywords:** typhoid fever, anti-typhoid herbal medicinal formulations, active plant
31 constituents

32 **List of abbreviations:** nontyphoidal Salmonella (NTS)

33 1. Introduction

34 Typhoid fever, a common and sometimes fatal infection of both adults and children that
35 causes bacteremia and inflammatory destruction of the intestine and other organs, is endemic
36 in countries, especially throughout Asia and Africa [1]. Chloramphenicol has been the
37 treatment of choice for typhoid fever for 40 years, but the widespread emergence of multi-
38 drug resistant *Salmonella typhi* (resistant to ampicillin, chloramphenicol, and trimethoprim-
39 sulfamethoxazole) has necessitated the search for other therapeutic options [2]. Currently
40 ciprofloxacin is the drug of choice in the treatment of enteric fever in Ghana. Alternatives
41 such as azithromycin and ceftriazone are also recommended [3].

42 Typhoid fever, caused by the bacterium *Salmonella enterica* serovar typhi (*S. typhi*), has
43 become rare in industrialized countries, yet it remains a major cause of enteric disease in
44 children in developing countries [1], resulting in an estimated incidence of 50 cases per
45 100,000 persons per year, predominantly in young school-age children [4]. Globally, it is
46 estimated that typhoid accounts for 16 million cases each year, resulting in over 600,000
47 deaths [5]. Typhoid fever therefore continues to be a public health problem in sub-Saharan
48 Africa. The disease is common in developing countries and concomitant with poor public
49 health and low socio economic indices [6]. Residents of poor communities lacking good
50 water and sanitation system are those mostly affected. It is estimated that a total of 400,000
51 cases occur annually in Africa, an incidence of 50 per 100,000 persons per year [7, 8].

52 In Sub-Saharan Africa invasive nontyphoidal salmonella (NTS) is also a major cause of
53 bacteremia in adults and children with an estimated occurrence of 175-388 cases per 100,000
54 children and 200-7500 cases per 100,000 HIV infected adults annually. In Ghana, typhoid
55 fever ranks among the leading 20 causes of outpatient illness, accounting for 0.92 % of
56 hospital admissions [9].

57 It is estimated that over 80 % of people in developing countries use herbal medicines for their
58 primary healthcare [10]. As many as 70% of Ghana's population is estimated to rely on
59 traditional medicine for their primary healthcare [11]. Correspondingly, majority of patients
60 in Ghana patronize herbal medicines for the treatment of typhoid fever, hence the availability
61 of a wide range of herbal medicines used in the treatment of typhoid fever. Concomitantly,
62 these same medicines are very often used to treat other common ailments such as malaria,
63 jaundice etc.

64 The widespread patronage of these herbal medicines explains the high rate of advertisements
65 of these products on radio, television and other social media. There is an estimated one
66 traditional medicine practitioner for every 400 people, compared to one allopathic doctor for
67 every 12,000 people, hence majority of the people patronize herbal medicines for the
68 management of various disease conditions [11]. Most of the herbal preparations are produced
69 and marketed by traditional medicine practitioners, they therefore have to be recommended
70 for providing healthcare to Ghanaian indigenes long before the advent of modern medicine.
71 This study therefore sought to determine the various types of herbal medicinal formulations
72 used in the treatment of typhoid fever on the Ghanaian market and appraises these products
73 via their product labels.

74 2. Methods

75 2.1. Drug collection

76 Between the periods of January – March of 2016, fifteen Pharmacies and six Herbal
77 Medicines Retail Shops within the Ga East Municipality, in the Greater Accra Region of
78 Ghana were visited and all herbal medicines indicated for the treatment of typhoid fever were
79 purchased. Only herbal medicines that had Food and Drugs Authority of Ghana registration
80 numbers were bought. Those without registration numbers were however noted. Sampling
81 was stopped when no new anti-typhoid formulations were being discovered.

82 2.2. Sampling Site

83 All the herbal products were collected within Haatso, Dome and Ashongman communities
84 located within the Ga East Municipality of the Greater Accra Region of Ghana (5° 44' 17" N,
85 0° 11' 42" W 5.738056, -0.195). According to the Ghana Statistical Service, 2010 Population

86 and Housing Census on the Ga East Municipality, it is located at the northern part of the
87 Greater Accra Region and covers a land area of about 85.7 square kilometers. The population
88 is almost 148,000. Males constitute 49% and females represent 51%. It has 40.3% of the
89 population below 20 years. The population density of the Ga Municipal area stands at 1,725
90 persons per square kilometer. Households in the Municipal Area are more of extended family
91 (56.2%) than nuclear family (43.8%). Almost 97.5 % of the population in the Municipal Area
92 is Ghanaians. Nearly 60% are literate. Of the employed population, 35.1% are engaged as
93 service and sales workers while 22.6% are craft workers and traders [12].

94

95 2.3. Appraisal of product labels

96 The products were given unique identification codes and were appraised with regard to
97 contents on their labels. Information used to assess the product labels included the presence
98 or absence of Food and Drugs Authority of Ghana registration numbers, place of
99 manufacture, type of formulation (solid or liquid), the plant and/or non-plant constituents
100 present, the adult dosage per day, the various indications and duration of treatment and the
101 contraindications. Data were analyzed in Microsoft Excel and have been presented as graphs.
102 The acceptable scientific names of the active plants constituents as stated on the product
103 labels were determined by searching in online taxonomic sources such as The Plant List
104 (TPL) (<http://www.theplantlist.org/>) and International Plant Name Index (www.ipni.org).

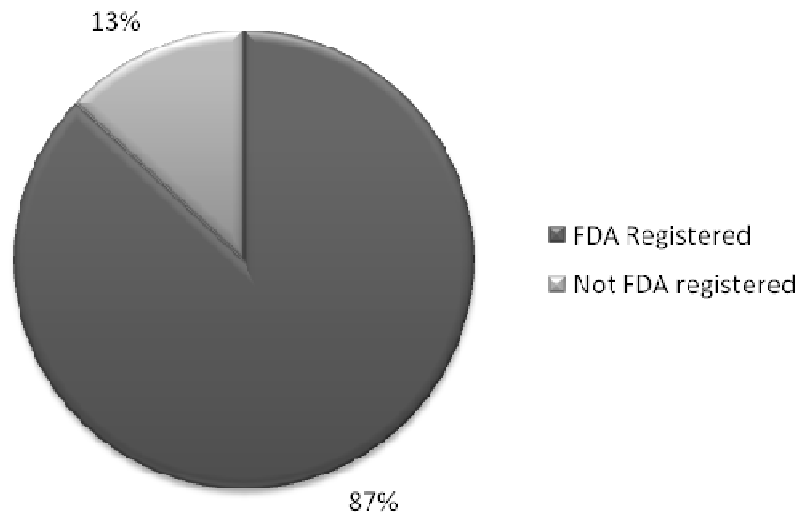
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106 3.0. Results

107 Of all the anti-typhoidal finished formulations sampled from the market, most had been
108 registered by the Food and Drugs Authority of Ghana, and this was indicated by the presence
109 of registered numbers on the products. Figure 1 below, displays the percentage of products
110 that had Food and Drugs Authority of Ghana registered numbers and those that did not have
111 them.

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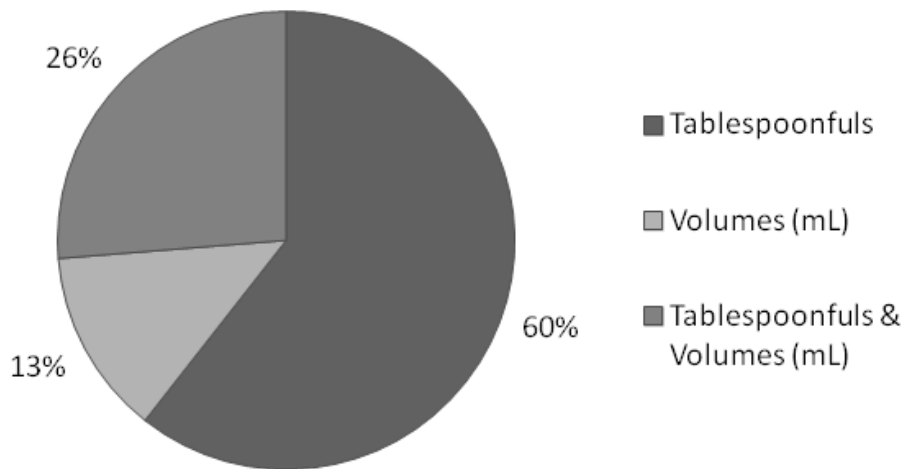


114

115 **Figure 1:** Proportion of Anti-typhoidal herbal medicinal products sold within the Ga East
 116 Municipality having **Food and Drugs Authority of Ghana** registered numbers and those that
 117 did not have, as percentage of the number of product (n = 16).

118 The cost of these herbal preparations ranged from 7 to 15 Ghana Cedis, with an average cost
 119 of 10 Ghana Cedis per product. All the herbal preparations were formulated as liquid
 120 decoctions, ranging from 180 mL to 1000 mL volumes. The adult daily doses on these
 121 products ranged from 45 mL to 300 mL with an average volume of 157 mL to be consumed
 122 daily. Measurements of the daily doses were stated as tablespoonfuls, millilitres or in most
 123 instances a combination of both tablespoonfuls and millilitres. Figure 2 below, summarizes
 124 the percentage of products labeled as such.

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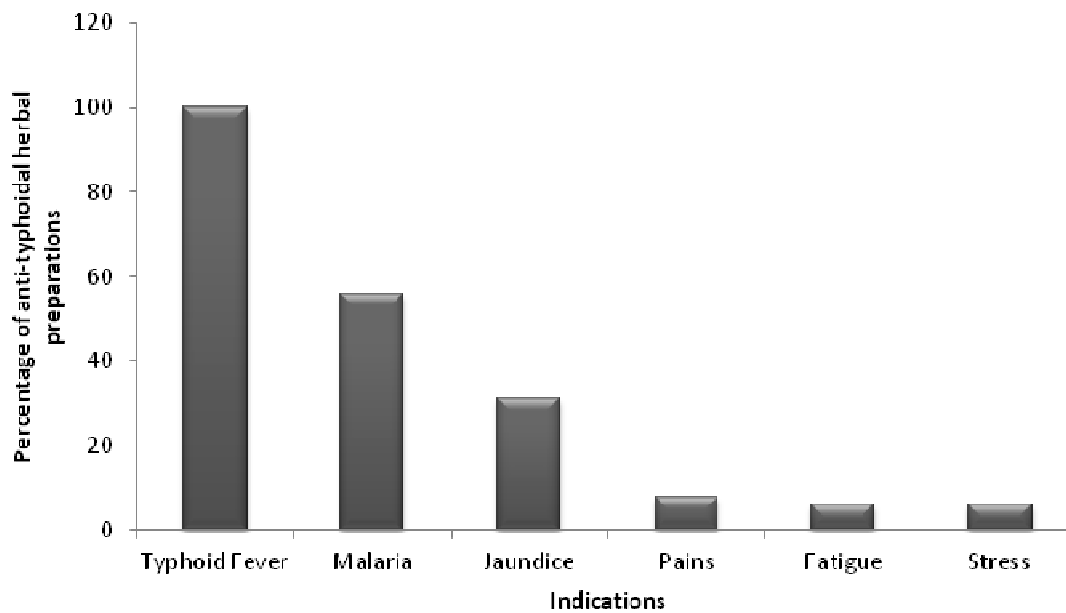


126

127 **Figure 2:** Measurement of doses of anti-typhoid herbal formulations; tablespoonfuls,
 128 volumes (mL) or stated as both tablespoonfuls and volumes (mL). Results presented as
 129 percentage of the total number of products (n = 16).

130 All the products encountered on the market were locally manufactured within the country
 131 (Ghana), with 71 % being manufactured in Accra and the other 19 % being manufactured
 132 within the Ashanti Region of Ghana.

133 The duration of treatment as indicated on the product label ranged from one to three weeks.
 134 The duration of treatment was not stated on 38% of the products. The herbal preparations
 135 sold for the treatment of typhoid was in all cases simultaneously used to treat at least one
 136 other disease condition, namely malaria, jaundice, pains (body pains, menstrual pains and
 137 headache), fatigue and stress. Figure 3 displays the percentage of these products that were
 138 indicated for the simultaneous treatment of particular conditions. On 56% of the products,
 139 indications for the treatment of malaria were also made, while on 31% of the products,
 140 treatment of jaundice was also recommended.



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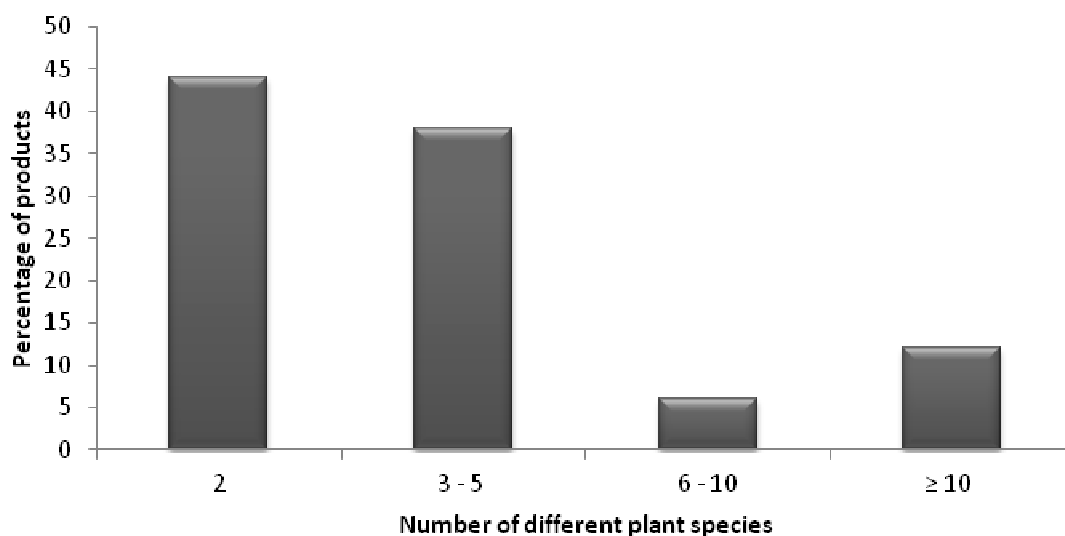
142 **Figure 3:** Indications for which anti-typhoidal herbal medicinal preparations were
 143 recommended.

144 An assessment of the contraindications for these products showed that all the products were
 145 contraindicated in pregnancy, lactating mothers and children below either 6 yrs or 12 yrs of
 146 age. No other groups of people were indicated as being contraindicated.

147 On all the products, the active components were stated to be plant extracts. No artificial
 148 constituents or excipients in the form of preservatives, flavours or sweeteners were indicated
 149 to be present.

150 The number of different plant species used to formulate these products ranged from two to
 151 twelve different plants. The products contained an average of four different plants species per
 152 formulation. Figure 4 displays a breakdown of the percentage of products containing the
 153 different number of plant species. Some particular plant species were identified to be present
 154 in a number of these formulated products while others were unique to only one product.
 155 Table 1 below contains the various plant species identified in the herbal preparations. A total
 156 of 39 plant species belonging to 25 families were identified to be used for the formulation of
 157 herbal medicines used for treatment of typhoid fever in Ghana.

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159

160 **Figure 4:** Distribution of number of plant species in products.

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163 **Table 1:** Active plant constituents in anti-typhoid herbal medicinal formulations. Group I
 164 (very frequently occurring plant species, recorded more than 3 - 6 times on the products) and
 165 Group II (less frequently occurring plant species, recorded 1-2 times on the products).

| Group I | |
|---|---|
| <i>Carica papaya</i> L. (family Caricaceae) | <i>Morinda lucida</i> Benth. (family Rubiaceae) |
| <i>Citrus aurantifolia</i> (family Rutaceae) | <i>Vernonia amygdalina</i> Delile. (family Compositae) |
| <i>Azadirachta indica</i> A. Juss (family Meliaceae) | <i>Cassia alata</i> L.(family Caesalpiniaceae) |
| <i>Khaya senegalensis</i> (Desv.) A. Juss (family Meliaceae) | <i>Momordica charantia</i> L. (family Cucurbitaceae) |
| Group II | |
| <i>Persea americana</i> Mill. (family Lauraceae) | <i>Cocos nucifera</i> L. (family Araceae) |
| <i>Phyllanthus fratenus</i> G.L. Webster (family Phyllanthaceae) | <i>Khaya ivorensis</i> A. Cheo (family Meliaceae) |
| <i>Trema orientalis</i> L. Blume (family Cannabaceae) | <i>Cryptolepis sanguinolenta</i> (Lindl.) Schltr (family Apocynaceae) |
| <i>Psidium guajava</i> L. (family Myrtaceae) | <i>Cymbopogon citrates</i> DC. (family Apocynaceae) |
| <i>Pycnanthus angolensis</i> (Welw.) Warb, (family Myristicaceae) | <i>Lantana camara</i> L. (family Verbanaceae) |
| <i>Rauwolfia vomitoria</i> Afzel (family Anarcadiaceae) | <i>Mangifera indica</i> L. (family Anarcadiaceae) |

| | |
|--|--|
| <i>Spondiasis mombin</i> L.(family Anacardiaceae) | <i>Cassia sieberiana</i> DC. (family Leguminosae) |
| <i>Carapa procera</i> DC. (family Meliaceae) | <i>Nauclea latifolia</i> Sm. (family Rubiaceae) |
| <i>Bidens pilosa</i> L. (family Asteraceae) | <i>Ocimum viride</i> Willd.(family Lamiaceae) |
| <i>Alstonia boonei</i> De Wild (family Apocynaceae) | <i>Paullina pinata</i> (family Sapindaceae) |
| <i>Aloe schweinfurthii</i> Baker (family Aloaceae) | <i>Zingiber officinale</i> Roscoe (family Zingiberaceae) |
| <i>Ocimum gratissimum</i> (family Lamiaceae) | <i>Cnestis ferruginea</i> Vahl ex DC.(family Connarceae) |
| <i>Cassia siamea</i> Lam.(family Caesalpiniaceae) | <i>Vitex grandifolia</i> Gürke (family Lamiaceae) |
| <i>Anthocleista nobilis</i> G. Don (family Gentianaceae) | |

166

167 Several errors in the names of the active plant constituents were discovered. A number of
168 plant names on the product labels could not be readily identified or were wrongly spelt. Some
169 labels mentioned only the plant genus but failed to state the particular species. After online
170 verification of the plant names, literature search showed that out of the 39 plants identified,
171 anti-typhoid activity has been documented for at least 89% (32), (Table 2).

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173

174 **Table 2. Literature review on plants**

| Species | Cross-reference |
|---------------------------------------|--|
| <i>Aloe schweinfurthii</i> | No reference found. |
| <i>Alstonia boonei</i> | The ethanol extract of this plant showed better antibacterial activity than the water, methanol and hexane extracts against <i>S. typhi</i> [13]. |
| <i>Anthocleista nobilis</i> G. Don | <i>A. nobilis</i> is commonly used for treating typhoid fever, amongst several other diseases in North-Central Nigeria [14]. |
| <i>Anthocleista vogelii</i> | Both the ethanol and aqueous extracts of the leaves had good antibacterial effect against <i>S. typhi</i> when compared to Chloramphenicol [15]. |
| <i>Azadirachta indica</i> | When the antibacterial activity of <i>A. indica</i> (Neem) was evaluated, the methanolic leaf extracts showed the highest zone of inhibition against salmonella as compared to other extracts [16]. |
| <i>Bidens pilosa</i> | <i>B. pilosa</i> is part of a number of plant species traditionally used in the management of typhoid fever in the Bamboutos Division of the West Region of Cameroon [17]. |
| <i>Carapa procera</i> | <i>C. procera</i> is part of the Cameroonian pharmacopeia which when evaluated against gastroenteritis-causing bacteria including <i>S. typhi</i> , the crude extracts and methanolic fractions of the leaves and bark |

| | |
|--|---|
| | were active against four (4) bacterial species including <i>S. typhi</i> and <i>S. paratyphi</i> . Active extracts and fractions gave MICs ranging from 2.5 to 10 mg/mL [18]. |
| <i>Carica papaya</i> | The seeds of <i>C. papaya</i> are effective against <i>E. coli</i> , <i>Salmonella</i> and <i>Staphylococcus</i> infections, where the leaf and stem extracts have demonstrated high activities against Gram negative bacteria and Gram positive bacteria, with the highest activity demonstrated against <i>S. typhi</i> . This study therefore recommended that <i>C. papaya</i> may be used for the treatment of gastroenteritis, urethritis, otitis media, typhoid fever and wound infections [19]. |
| <i>Cassia alata</i> (<i>Senna alata</i>) | The Bamboutos division in Cameroon uses this plant in the treatment of typhoid. This plant showed the highest zones of inhibition with diameter of 24, 22.5 and 20.5 mm against <i>S. paratyphi A</i> , <i>S. paratyphi B</i> and <i>S. typhi</i> respectively at 160 mg/mL concentration [20]. |
| <i>Cassia siamea</i> (<i>Senna siamea</i>) | The ethanol and ethyl acetate extracts showed inhibition against <i>S. typhi</i> [21]. |
| <i>Cassia sieberiana</i> | Ethanol and chloroform extracts of the leaves of <i>C. siberiana</i> showed activity against <i>S. typhi</i> at 100 mg/mL. |
| <i>Citrus aurantifolia</i> | This plant is widely used in West Africa for its antimicrobial activity against gastrointestinal pathogens including <i>Salmonella</i> [22, 23]. |
| <i>Cnestis ferruginea</i> | The ethanol extracts of the stem of <i>C. ferruginea</i> demonstrated activity against various bacteria including <i>Salmonella</i> . MIC and MBC against the bacterial isolates were in the range of 3.2 – 6.3 mg/mL [24]. |
| <i>Cocos nucifera</i> | <i>C. nucifera</i> mesocarp powder showed very high activity against <i>Salmonella typhi</i> [25]. |
| <i>Cryptolepis sanguinolenta</i> | A 2 mg/mL each of 70% ethanol, hot and cold aqueous extract of <i>C. sanguinolenta</i> exhibited activity against <i>S. typhimurium</i> , three strains each of <i>Salmonella typhi</i> and several other microorganisms [26]. |
| <i>Cymbopogon citratus</i> | <i>C. citrates</i> was documented in an ethnomedicinal survey of plants used for the treatment of typhoid fever in Ijebu Ode Local Government Area of Ogun State Nigeria [27]. It was also observed in another study to possess high antimicrobial activity against <i>S. typhi</i> [28]. |
| <i>Khaya senegalensis</i> | The ethanol and aqueous extracts of the stem bark extracts of <i>K. senegalensis</i> showed activity against <i>S. typhi</i> at a concentration of 50 mg/mL with an inhibition zone of 15 mm respectively [29]. |
| <i>Khaya ivorensis</i> | It was observed that when mixed with black peppercorns it can be used to treat diarrhea and dysentery. A bark decoction is used as a drink or bath for back pains and as a lotion for rheumatism. [30] |
| <i>Lantana camara</i> | <i>L. camara</i> has activity against <i>S. gallinarum</i> with MIC starting at 5 mg/mL [31]. |
| <i>Mangifera indica</i> | Aqueous extract of <i>M. indica</i> showed good anti-salmonella activity against clinical isolates of <i>S. typhus</i> , with 98.8% inhibition at 200 µg/mL concentration. IC50 required for killing <i>Salmonella</i> ranged from 101.3 to 800 µg/mL [32], other studies have also supported the anti-typhoid activity of this plant [33]. |

| | |
|------------------------------|---|
| <i>Momordica charantia</i> | Marked reduction in infection level was observed in rats treated with extracts from <i>M. charantia</i> when compared to standard drugs [34]. |
| <i>Morinda lucida</i> | The water and chloroform extracts of leaves of <i>M. lucida</i> has produced antibacterial effects comparable to those of standard antibiotics against <i>S. typhi</i> and other microorganism [35]. The stem bark, roots and leaves infusions are also documented to be used as an anti-dysentery [36]. |
| <i>Nauclea latifolia</i> | The aqueous and alcoholic extracts of the leaves and roots of <i>N. latifolia</i> showed no appreciable inhibitory effect against <i>S. typhi</i> [37]. |
| <i>Ocimum gratissimum</i> | The steam distillation extract of <i>O. gratissimum</i> has shown activity at 0.01% against <i>S. typhimurium</i> and 0.001% against <i>S. typhi</i> [38]. |
| <i>Ocimum viride</i> | <i>Ocimum viride</i> is also known as <i>Ocimum gratissimum</i> and the antibacterial potential of cold water, hot water (100°C), ethanol and chloroform extracts of <i>Ocimum gratissimum</i> leaves were tested against some pathogenic bacteria known to cause diaorrhoea; <i>Staphylococcus aureus</i> , <i>Escherichia coli</i> , <i>Shigella sp.</i> and <i>Salmonella sp.</i> [39] |
| <i>Paullina piñata</i> | The African continent has a very rich biodiversity and many plants are used for therapeutic purposes. Over 5,000 different species of plant substances have been recognized to occur in these areas, and many of them have been found to be useful in traditional medicine for prophylaxis and cure of diseases. [40, 41] |
| <i>Persea americana</i> | The ethyl acetate, chloroform and methanol extracts did not demonstrated pronounced activity against <i>S. typhi</i> [42]. |
| <i>Phyllanthus fraternus</i> | The methanol extract of the root of <i>P. fraternus</i> showed maximum antibacterial activity against <i>S. typhi</i> B with a zone of inhibition of 11 mm and minimum activity against <i>S. typhi</i> A, with zone of inhibition of 10 mm [43]. |
| <i>Psidium guajava</i> | The administration of 10-30 mg/100g of the aqueous extract of <i>P. guajava</i> to <i>S. typhi</i> infected rats over 12 h through the oral route produced a recovery within seven days [44]. |
| <i>Pycnanthus angolensis</i> | Methanol leaf extract caused inhibition against <i>Salmonella</i> [45]. |
| <i>Rauwolfia vomitoria</i> | <i>R. vomitoria</i> has a lot of medical potential in curing and preventing ailments including typhoid [46]. |
| <i>Spondiasis mombin</i> | The aqueous and organic solvents extract of fresh leaves of <i>S. mombin</i> exhibited anti-microbial activity against <i>S. typhi</i> [47]. |
| <i>Trema orientalis</i> | Ethnomedicinal studies on <i>Trema orientalis</i> Linn. Blume (Ulmaceae) have shown that it is used by traditional practitioners to treat several ailments viz. diabetes mellitus, respiratory diseases, oliguria, and malaria. [48, 49] |
| <i>Vernonia amygdalina</i> | Aqueous, ethanol and acetone extracts of <i>V. amygdalina</i> leaf, stem and roots were tested at a concentration of 100 mg/mL against antibiotic-resistant <i>Salmonella</i> species. Aqueous extracts of the leaf, stem and roots showed no activity against antibiotic resistant <i>Salmonella</i> isolate, while the ethanol and acetone extracts showed activity rates of 20% and 17% for roots, 14.3% and 12.9% for stem, |

| | |
|----------------------------|--|
| | and, 15.7% and 11.4% for leaf [44]. The anti-Salmonella activity has been further confirmed by the ethanolic extract [50, 51]. |
| <i>Vitex grandifolia</i> | Ethanol extracts demonstrated broad spectrum antibacterial activity against Salmonella [52]. |
| <i>Zingiber officinale</i> | Soybean oil extract of ginger showed high zone of inhibition (11.67±1.53 mm) against <i>Salmonella</i> spp [53] |

175

176 **4. Discussion**

177 The wide spread use of herbal medicines in the treatment of typhoid in Ghana is a small
 178 indication of how widespread herbal medicines are used in Ghana. An estimated 80 % of
 179 rural villagers in southern Ghana rely on plants as their main medicinal source [54]. The
 180 widespread use of herbal medicines in the coastal areas of Ghana, which includes Accra is
 181 attributed to rapid urbanization in an area with a high level of endemic plant taxa and a
 182 population heavily dependent on herbal medicines for their primary health care [55].

183 The fact that all these products were manufactured locally could be indications of how
 184 traditional herbal medicines are widely used within this area and the widespread belief in the
 185 efficacy of these herbs. This may also indicate the high level of patronage of these products
 186 and the availability of the various plant species used in the production of these products. All
 187 the products were formulated as liquid decoctions. This could be indicative of probably the
 188 preference for liquid formulation by the consumers or as a result of the manufacturers lacking
 189 sophisticated techniques to produce the other dosage forms. Most manufacturers of herbal
 190 medicines in Ghana are believed to be small to medium scale businesses.

191 The daily dosage of these products ranged from 45 to 300 mL. These daily volumes are quite
 192 high, and may be an indication that the products can be better formulated so that the daily
 193 doses are smaller in volumes. This may require standardization of the preparation to increase
 194 the concentration of the active ingredients in the final products and improve the quality [56].
 195 This will result in a decrease in the final product volumes which currently ranges from 180 –
 196 1000 mL. Only two out of the 16 products provided measuring cups. A lack of standardized
 197 measuring instruments will promote inaccurate measurement of the medicines. Measuring
 198 spoons and cups can probably be included in all the products and the dosage stated in
 199 millilitres to enhance accurate measurement of doses [57].

200 The cost of these herbal preparations ranged from 7 to 15 Ghana Cedis, with an average cost
201 of 10 Ghana Cedis per product. It is generally believed that herbal medicines are inexpensive
202 [58], however, for most of these products more than one bottle of medication will need to be
203 taken before one can complete the recommended duration of treatment. Hence a critical cost
204 analysis will need to be made to really determine whether the costs of these herbal
205 preparations are lower or higher when compared to the available alternative orthodox drugs
206 such as ciprofloxacin which is the drug of choice for treating typhoid in Ghana [3].

207 The duration of treatment as indicated on the product labels ranged from one to three weeks.
208 On 38 % of the products, the duration of treatment was not stated at all. This puts the patient
209 at a high risk of either under dosage or over dosage of the medicine. Under dosage could lead
210 to treatment failure and over dosage may increase the chance of toxicity. An assessment of
211 the duration of treatment and the daily dosage showed that majority of these products will
212 need more than one product to be able to complete the recommended duration of treatment.

213 The anti-typhoid herbal formulations were simultaneously used for the treatment of malaria,
214 jaundice, pains (body pains, menstrual pains and headache), fatigue and stress. A lot of
215 Ghanaians accept that one herbal medicine could be the cure for many ailments and this
216 notion may be the reason for which high numbers of plant species (up to 12) is found in each
217 formulation. An average of 4 different plant species was used in formulating these products.
218 The inclusion of several plants could mean that the products were probably formulated to
219 multipurposely treat several ailments. Some plants on their own are also multi-purpose
220 medicinal plants [59]. *Azadirachta indica* [54], *Vernonia amygdalina* [60], *Momordica*
221 *charantia* [61] etc., are all plants documented to have multipurpose medicinal actions and
222 available in these preparations.

223 The presence of a wide range of plant species [40] give a snapshot of the country's medicinal
224 flora and, reflect the concerns about health and illness and the importance of traditional
225 medicine among Ghanaians [62]. However, mistakes in the names of the plant species will
226 need to be critically checked to aid in correct identification of the components.

227 In Ghana, typhoid fever ranks among the leading 20 causes of outpatient illness, accounting
228 for 0.92% of hospital admissions [9]. Malaria on the other hand remains hyper endemic in
229 Ghana and is the single most important cause of mortality and morbidity especially among

230 children under five years, pregnant women and the poor [63]. These are therefore two
231 prevalent infections in Ghana. The rationale to combine several active plants extracts is in
232 itself not a bad idea since some plant species may also have been combined in these
233 preparations to enable the individual components work synergistically to increase the overall
234 effectiveness of the preparation. In traditional medicine whole plants extracts or mixtures of plants
235 are used rather than isolated compounds. There is evidence that some crude plant extracts have greater
236 *in vitro* or/and *in vivo* activities than isolated constituents at an equivalent dose [64]. Studies will
237 however have to be conducted on these herbal formulations to ascertain stability of the active
238 components, physical and chemical interactions between the various components and safety
239 in consuming such high numbers of different extracts (compounds). On the average, each
240 plant extract may contain several of chemical compounds.

241 From another perspective, these plants extracts may be combined because the manufacturers
242 may have very little or no clue as to the active components of the extracts. It may therefore be
243 recommended that bioactivity-guided isolation and characterization be performed on these
244 formulations to identify the possible active plant fractions or compounds. This will result in
245 the exclusion of unnecessary or harmful compounds or fractions from the formulation. This
246 will make the resulting formulation safer for consumers to use and even more effective in the
247 treatment of typhoid due to higher concentrations of the active ingredients.

248 An assessment of the contraindications showed that all the products were contraindicated in
249 pregnancy, lactating mothers and children below either 6 yrs or 12 yrs old. This is very useful
250 in preventing possible toxicity in such vulnerable groups since very little or no toxicity
251 studies may have been conducted in these sensitive groups of patients to ascertain the product
252 safety. However due to the wide patronage of these products, both acute and chronic toxicity
253 studies may need to be conducted in other groups of patients. This will also ascertain the
254 safety of these products when used in other co-morbid conditions and age groups.

255 No artificial constituents whether in the form of active constituents and inactive constituents
256 such as preservatives, flavours or sweeteners were indicated to be present in the products.
257 This may raise the question as to whether the components of these formulations are anti-
258 microbially active enough to preserve the products for their respective shelf lives and during
259 the usage period. All the products were aqueous based and hence the high concentration of
260 water makes them very prone to microbiological contamination not to mention the high

261 incidence of the presence of several microbial pathogens in herbal products and their toxins
262 [65].

263 A literature search performed on documented anti-typhoid activity of the plants used in
264 formulating these preparations such as (*Carica papaya* [66], *Vernonia amygdalina* [67-69],
265 *Morinda lucida* [35,36], *Azadirachter indica* [16] and *Citrus aurantifolia* [23] etc.) showed
266 that their inclusion as active ingredients may be well justified.

267 A further literature search on the phytochemical constituents of the plants with the highest
268 frequency *Carica papaya*, *Morinda lucida*, *Citrus aurantifolia*, *Vernonia amygdalina*,
269 *Azadirachta indica*, *Khaya senegalensis*, *Cassia alata* and *Momordica charantia* (Group I,
270 Table 1) showed that all the 8 plants contained flavonoids, while 7 contained alkaloids, 6 out
271 of the eight plants contained tannins, saponins and glycosides as secondary metabolites [70-
272 77]. The antityphoid activity may well be due to the presence of these phytoconstituents, but
273 further studies may need to be done to ascertain this.

274 5. Conclusions

275 The active plant components of the anti-typhoidal formulations seem to be well justified and
276 probably indicate that the resulting products could be highly active. The labeling of these
277 products can also be improved in respect of the names of the active components and directive
278 for dosage. Improvement can also be made in terms of formulation of the products to reduce
279 the daily dosage and product volumes.

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