

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

73 **2. Methods**

74 **2.1. Drug collection**

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

81 **2.2. Sampling Site**

82 All the herbal products were collected within Haatso, Dome and Ashongman communities
83 located within the Ga East Municipality of Accra Ghana (5° 44' 17" N, 0° 11' 42"
84 W5.738056, -0.195). According to the Ghana Statistical Service, 2010 Population and
85 Housing Census on the Ga East Municipality, it is located at the northern part of the Greater

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

93

94 **2.3. Appraisal of product labels**

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

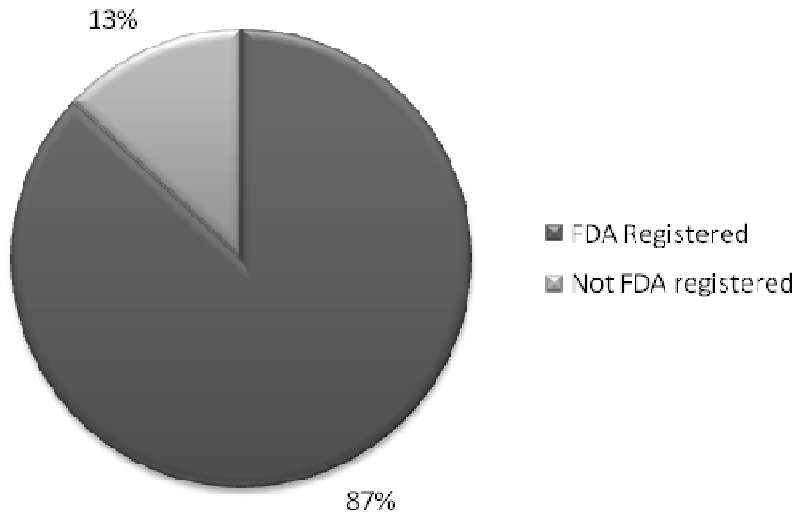
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105 **3.0. Results**

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

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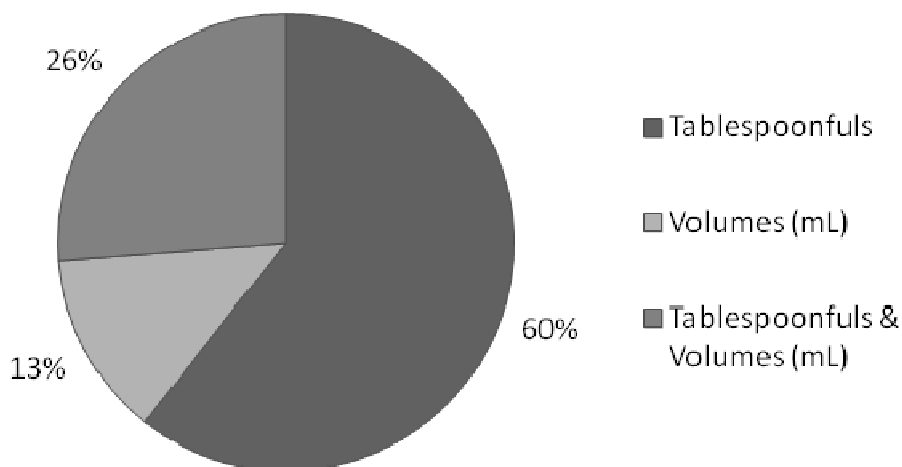


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113 **Figure 1:** Proportion of Anti-typhoidal herbal medicinal products sold within the Ga East
 114 Municipality having Food and Drugs Authority of Ghana registered numbers and those that
 115 did not have, as percentage of the number of product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

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

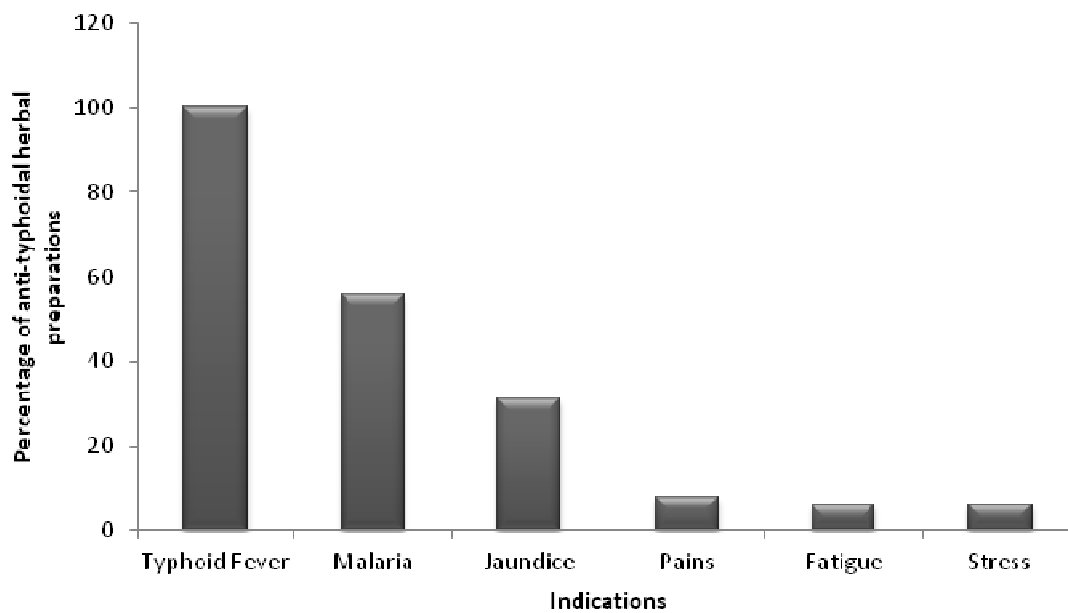
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125 **Figure 2:** Measurement of doses of anti-typhoid herbal formulations; tablespoonfuls,
 126 volumes (mL) or stated as both tablespoonfuls and volumes (mL). Results presented as
 127 percentage of the total number of products (n = 16).

128 All the products encountered on the market were locally manufactured within the country
 129 (Ghana), with 71 % being manufactured in Accra and the other 19 % being manufactured
 130 within the Ashanti Region of Ghana. The duration of treatment as indicated on the product
 131 label ranged from one to three weeks. On 38 % of the products, the duration of treatment was
 132 not stated at all. The herbal preparations sold for the treatment of typhoid was in all cases
 133 simultaneously used to treat at least one other disease condition, namely malaria, jaundice,
 134 pains (body pains, menstrual pains and headache), fatigue and stress. Figure 3 displays the
 135 percentage of these products that were indicated for the simultaneous treatment of particular
 136 conditions. On 56 % of the products, indications for the treatment of malaria were also made,
 137 while on 31 % of the products, treatment of jaundice was also recommended.



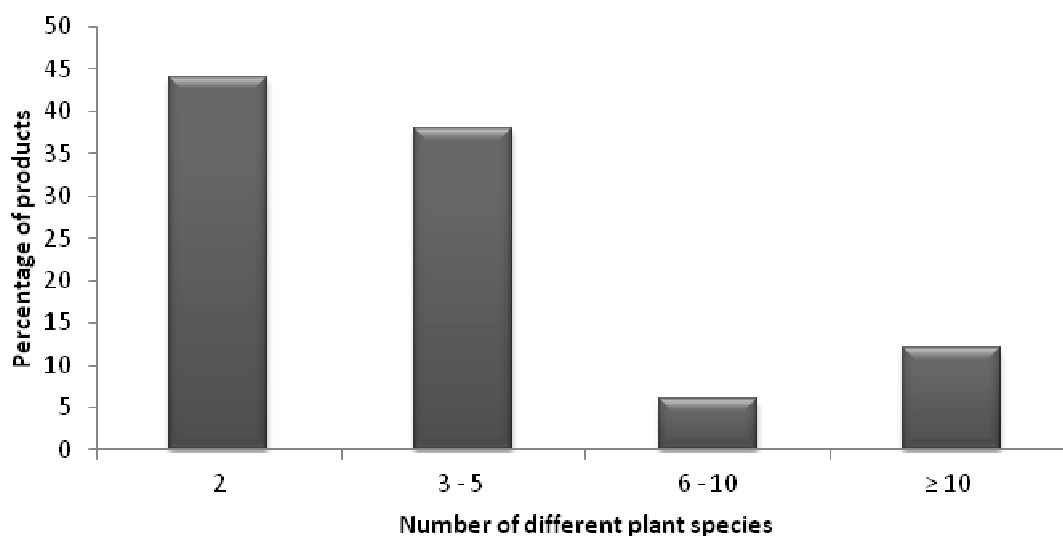
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139 **Figure 3:** Indications for which anti-typhoidal herbal medicinal preparations were
 140 recommended.

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

144 Of all the products (100 %) that were appraised, the active components were stated to be
 145 plant extracts. No artificial constituents or excipients in the form of preservatives, flavours or
 146 sweeteners were indicated to be present. The number of different plant species used to
 147 formulate these products ranged from two to twelve different plants. The products contained
 148 an average of four different plants species per formulation. Figure 4 displays a breakdown of
 149 the percentage of products containing the different number of plant species. Some particular
 150 plant species were identified to be present in a number of these formulated products while
 151 others were unique to only one product. Table 1 below contains the various plant species
 152 identified in the herbal preparations. A total of 39 plant species belonging to 25 families were
 153 identified to be used for the formulation of herbal medicines used for treatment of typhoid
 154 fever in Ghana.

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156

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

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160 **Table 1:** Active plant constituents in anti-typhoid herbal medicinal formulations. Group I
 161 (very frequently occurring plant species, recorded more than 3 - 6 times on the products) and
 162 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 viridi</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)	

163

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

169

170

171 **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 barks

	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. While 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>	Reference not found.
<i>Lantana camara</i>	<i>L. camara</i> has activity against <i>S. gallinarum</i> with MIC starting at 5 mg/mL [30].
<i>Mangifera indica</i>	Aqueous extract of <i>M. indica</i> showed good antisalmonella activity against clinical isolates of <i>S. typhi</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 [31], other studies have also supported the anti-typhoid activity of this plant [32].
<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 [33].

<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 [34]. The stem bark, roots and leaves infusions are also documented to be used as an anti-dysentery [35].
<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> [36].
<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> [37].
<i>Ocimum viride</i>	Reference not found.
<i>Paullina piñata</i>	Reference not found.
<i>Persea americana</i>	The ethyl acetate, chloroform and methanol extracts did not demonstrated pronounced activity against <i>S. typhi</i> [38].
<i>Phylanthus 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 [39].
<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 [40].
<i>Pycnanthus angolensis</i>	Methanol leaf extract caused inhibition against <i>Salmonella</i> [41].
<i>Rauwolfia vomitoria</i>	<i>R. vomitoria</i> has a lot of medical potential in curing and preventing ailments including typhoid [42].
<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> [43].
<i>Trema orientalis</i>	Reference not found.
<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- <i>Salmonella</i> activity has been further confirmed by the ethanolic extract [45].
<i>Vitex grandifolia</i>	Ethanol extracts demonstrated broad spectrum antibacterial activity against <i>Salmonella</i> [46].
<i>Zingiber officinale</i>	Soybean oil extract of ginger showed high zone of inhibition (11.67±1.53 mm) against <i>Salmonella</i> spp [47].

172

173 4. Discussion

174 The wide spread use of herbal medicines in the treatment of typhoid in Ghana is a small
175 indication of how widespread herbal medicines are used in Ghana. An estimated 80 % of

176 rural villagers in southern Ghana rely on plants as their main medicinal source [48]. The
177 widespread use of herbal medicines in the Coastal areas of Ghana, which includes Accra is
178 attributed to rapid urbanization in an area with a high level of endemic plant taxa and a
179 population heavily dependent on herbal medicines for their primary health care [49]. The fact
180 that all these products were manufactured locally could be indications of how traditional
181 herbal medicines are widely used within this area and the widespread belief in the efficacy of
182 these herbs. This may also indicate the high level of patronage of these products and the
183 availability of the various plant species used in the production of these products. All the
184 products were formulated as liquid decoctions. This could be indicative of probably the
185 preference for liquid formulation by the consumers or as a result of the manufacturers lacking
186 sophisticated techniques to produce the other dosage forms. Most manufacturers of herbal
187 medicines in Ghana are believed to be small to medium scale businesses. The daily dosage of
188 these products ranged from 45 to 300 mL. These daily volumes are quite high, and may be an
189 indication that the products can be better formulated so that the daily doses are smaller in
190 volumes. This may require standardization of the preparation to increase the concentration of
191 the active ingredients in the final products and improve the quality [50]. This will result in a
192 decrease in the final product volumes which currently ranges from 180 – 1000 mL. Only two
193 out of the 16 products provided measuring cups, this will promote inaccurate measurement of
194 the medicines. Measuring spoons and cups can probably be included in all the products and
195 the dosage stated in millilitres to enhance accurate measurement of doses [51].

196 The cost of these herbal preparations ranged from 7 to 15 Ghana Cedis, with an average cost
197 of 10 Ghana Cedis per product. It is generally believed that herbal medicines are inexpensive
198 [52], however, for most of these products more than one bottle of medication will need to be
199 taken before one can complete the recommended duration of treatment. Hence a critical cost
200 analysis will need to be made to really determine whether the costs of these herbal
201 preparations are lower or higher when compared to the available alternative orthodox drugs
202 such as ciprofloxacin which is the drug of choice for treating typhoid in Ghana [3]. The
203 duration of treatment as indicated on the product labels ranged from one to three weeks. On
204 38 % of the products, the duration of treatment was not stated at all. This puts the patient at a
205 high risk of either under dosage or over dosage of the medicine. Under dosage could lead to
206 treatment failure and over dosage may increase the chance of toxicity. An assessment of the

207 duration of treatment and the daily dosage showed that majority of these products will need
208 more than one product to be able to complete the recommended duration of treatment.

209 The anti-typhoid herbal formulations were simultaneously used for the treatment of malaria,
210 jaundice, pains (body pains, menstrual pains and headache), fatigue and stress. A lot of
211 Ghanaians accept that one herbal medicine could be the cure for many ailments and this
212 notion may be the reason for which high numbers of plant species (up to 12) is found in each
213 formulation. An average of 4 different plant species was used in formulating these products.
214 The inclusion of several plants could mean that the products were probably formulated to
215 multipurposely treat several ailments. Some plants on their own are also multi-purpose
216 medicinal plants [53]. *Azadirachta indica* [54], *Vernonia amygdalina* [55], *Momordica*
217 *charantia* [56] etc., are all plants documented to have multipurpose medicinal actions and
218 available in these preparations. The presence of a wide range of plant species (36) give a
219 snapshot of the country's medicinal flora and, reflect the concerns about health and illness
220 and the importance of traditional medicine among Ghanaians [49]. However, mistakes in the
221 names of the plant species will need to be critically checked to aid in correct identification of
222 the components. In Ghana, typhoid fever ranks among the leading 20 causes of outpatient
223 illness, accounting for 0.92% of hospital admissions [9]. Malaria on the other hand remains
224 hyper endemic in Ghana and is the single most important cause of mortality and morbidity
225 especially among children under five years, pregnant women and the poor [57]. These are
226 therefore two prevalent infections in Ghana. The rationale to combine several active plants
227 extracts is in itself not a bad idea since some plant species may also have been combined
228 in these preparations to enable the individual components work synergistically to increase the
229 overall effectiveness of the preparation. In traditional medicine whole plants extracts or mixtures
230 of plants are used rather than isolated compounds. There is evidence that some crude plant extracts
231 have greater *in vitro* or/and *in vivo* activities than isolated constituents at an equivalent dose [58].
232 Studies will however have to be conducted on these herbal formulations to ascertain stability
233 of the active components, physical and chemical interactions between the various
234 components and safety in consuming such high numbers of different extracts (compounds).
235 On the average, each plant extract may contain several of chemical compounds. From another
236 reasoning, these plants extracts may be combined because the manufacturers may have very
237 little or no clue as to the active components of the extracts. It may therefore be recommended
238 that bioactivity guided isolation and characterization be performed on these formulations to

239 identify the possible active plant fractions or compounds. This will result in the exclusion of
240 unnecessary or harmful compounds or fractions from the formulation. This will make the
241 resulting formulation safer for consumers to use and even more effective in the treatment of
242 typhoid due to higher concentrations of the active ingredients. An assessment of the
243 contraindications showed that all the products were contraindicated in pregnancy, lactating
244 mothers and children below either 6 yrs or 12 yrs old. This is very useful in preventing
245 possible toxicity in such vulnerable groups since very little or no toxicity studies may have
246 been conducted in these sensitive groups of patients to ascertain the product safety. However
247 due to the wide patronage of these products, both acute and chronic toxicity studies may need
248 to be conducted in other groups of patients. This will also ascertain the safety of these
249 products when used in other co-morbid conditions and age groups.

250 No artificial constituents whether in the form of active constituents and inactive constituents
251 such as preservatives, flavours or sweeteners were indicated to be present in the products.
252 This may raise the question as to whether the components of these formulations are anti-
253 microbially active enough to preserve the products for their respective shelf lives and during
254 the usage period. All the products were aqueous based and hence the high concentration of
255 water makes them very prone to microbiological contamination not to mention the high
256 incidence of the presence of several microbial pathogens in herbal products and their toxins
257 [59].

258 A literature search performed on documented anti-typhoid activity of the plants used in
259 formulating these preparations such as (*Carica papaya* [60], *Vernonia amygdalina* [61-63],
260 *Morinda lucida* [34, 35], *Azadirachter indica* [16] and *Citrus aurantifolia* [23] etc.) showed
261 that their inclusion as active ingredients may be well justified.

262 A further literature search on the phytochemical constituents of the plants with the highest
263 frequency *Carica papaya*, *Morinda lucida*, *Citrus aurantifolia*, *Vernonia amygdalina*,
264 *Azadirachta indica*, *Khaya senegalensis*, *Cassia alata* and *Momordica charantia* (Group I,
265 Table 1) showed that all the 8 plants contained flavonoids, while 7 contained alkaloids, 6 out
266 of the eight plants contained tannins, saponins and glycosides as secondary metabolites [64-
267 71]. The antityphoid activity may well be due to the presence of these phytoconstituents, but
268 further studies may need to be done to ascertain this.

269 **5. Conclusions**

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

275 **Acknowledgements**

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277 collecting the herbal products, and also commend the Traditional Healers in Ghana who are
278 the main innovators of such products.

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