

1 **Bioactive compounds from Mangosteen fruit peels (*Garcinia mangostana* L.) and**  
2 **assessment of their antioxidant potential**

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24 **Abstract**

25 The aim of this study was to valorize mangosteen peels as a source of bioactive compounds for  
26 the treatment/prevention of cardiometabolic diseases. Peels from washed mature fruits of  
27 *Garcinia mangostana* were dried, crushed, and sieved, and the bioactive compounds were  
28 extracted using distilled water and ethanol 70%, and quantified. The antioxidant potential of  
29 the different extracts was assessed through their DPPH scavenging activity, iron reducing  
30 power, and total antioxidant capacity. Results showed that ethanol at 70% extracted more  
31 bioactive compounds compared to water. Total polyphenols content of 57.19 mg GAE/g DM,  
32 flavonoids of 35.06 mg QE/g DM, alkaloids of 4.49 mg QuiE/g DM, and vitamin C of 1.42  
33 mg/100g DM were obtained from hydroethanolic extract. As expected, the highest percentage  
34 of scavenging DPPH radical (85.98%) was recorded with hydroethanolic extract compared to  
35 the aqueous one (44.66%). Similar behaviors were noticed with the hydroethanolic extract  
36 regarding the iron-reducing capacity and the total antioxidant capacity. Thus, justifying the  
37 positive correlations obtained between bioactive compounds and antioxidant activities although  
38 significant ( $p < 0.05$ ) between alkaloids and DPPH scavenging activity. Mangosteen peels is a  
39 good source of bioactive compounds that might be potentially used for food preservation and  
40 the management of cardio-metabolic diseases.

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47 **Keywords:** Mangosteen, fruit, peels, valorization, bioactive compounds, antioxidant activity.

## 48 1 INTRODUCTION

49 Mangosteen (*Garcinia mangostana* L.) is a flowering plant belonging to the family Clusiaceae  
50 (Guttiferae) and the genus *Garcinia* (Nazre et al., 2018). Native from tropical Asia (Malaysia,  
51 Thailand and Indonesia), mangosteen produces rounded, purplish, golfball-sized fruits with a  
52 thick and very bitter peel (Marzaimi et al., 2019). The plant is mainly grown for its fruits which  
53 have a fine and delicious taste involving the mixture of acidity and sweetness (Aizat et al.,  
54 2019). The worldwide production of mangosteen fruits was estimated at 700,000 tons in 2017  
55 (Altendorf, 2018). The mangosteen culture was recently introduced in Cameroon, and  
56 successful trials were achieved in the agro-ecological zone of Njombé, Littoral Region (Journal  
57 de Gazelle, 2013). Although the mangosteen fruits are highly consumed in urban area, it still  
58 remains unknown by a large part of the population due to its recent introduction in the country.  
59 The fruits are generally used as functional food and in the formulation of medicines and  
60 cosmetics as they contain several bioactive compounds endowed with antioxidant properties  
61 (Foiklang et al., 2016). However, in Cameroon and elsewhere, the fruit pulps are of interest and  
62 the other parts of the fruits such as its peels are thrown in the nature where they constitute a  
63 potential source of environmental pollution. Currently, researches are directed towards the  
64 valorization of these parts of the fruits considered as wastes. In that order of idea, Ghasemzadeh  
65 et al. (2018) and Zadernowski et al. (2009) made a comparative study and found that the  
66 mangosteen fruit peels contained more bioactive compounds than its pulp. Purba et al. (2021)  
67 demonstrated the antioxidant activity of these bioactive compounds. In a recent study, it was  
68 suggested that the bioactive compounds from mangosteen fruit peels might play an important  
69 role in the management diabetes (type II) and obesity, in the prevention of fats accumulation  
70 (through induction of lipolysis and apoptosis in pre-adipocytes), and in the inhibition of  
71 pancreatic lipase (Watanabe et al., 2018).

72 Giving the composition and profile of bioactive compounds from plants vary according to the  
73 geographical areas of culture, it therefore appears necessary to know the content of bioactive  
74 compounds of the mangosteen fruit peels newly introduced and cultivated in Cameroon. It is in  
75 this context that the present research was designed. The main objective was to valorize the  
76 mangosteen fruit peels as a source of functional compounds endowed of biological properties.  
77 Specifically, it consisted to (i) extract and evaluate the bioactive compounds from mangosteen  
78 fruit peels, (ii) assess the antioxidant activity of these bioactive compounds, and (iii) determine  
79 the contribution of bioactive compounds in the antioxidant mechanism.

## 80 **2 MATERIALS AND METHODS**

### 81 *2.1 Chemicals*

82 All the reagents used in this study were of analytical grade and purchased from Merck  
83 (Germany). They included Folin-Ciocalteu, sodium carbonate, Ethanol 99%, gallic acid,  
84 aluminum chloride, potassium acetate, quercetin, iron chloride, hydrochloric acid, ascorbic  
85 acid, sulphuric acid, sodium dihydrogen phosphate, dibasic hydrogenophosphate, ammonium  
86 molybdate, potassium ferricyanide, trichloroacetic acid.

### 87 *2.2 Biological materials*

88 The mangosteen fruits were provided by the Agricultural Research Institute for Development  
89 (IRAD) of Njombé, agro-ecological zone No. 4 (4°33'15.89 N and 9°37'42.84 E), Littoral  
90 Region, Cameroon. They were identified at the National Herbarium with the voucher number  
91 No. 25 666. The fruits were washed twice with distilled water and the peels were manually  
92 separated from the pulp, carefully washed again, cut into thin slices of approximately 5 cm, and  
93 dried in an oven (Memmert, Germany) for 7 days at 60°C. The dried peels were crushed, sieved  
94 (500 µm), packed into polyethylene bags, weighed and stored at 4°C for analysis.

### 95 *2.3 Preparation of extracts*

96 Distilled water and a solution of ethanol at 70% (v/v) in distilled water were used as solvents  
97 to extract bioactive compounds from the powder of mangosteen fruit peels. In the protocol, 5  
98 g of powder was introduced into a 250 mL Erlenmeyer and 100 mL of solvent was added. The  
99 mixture was homogenized for 24 h at room temperature ( $25\pm 1^\circ\text{C}$ ) using a magnetic stirrer (Lab-  
100 Line, Pyro-Multi-Magnestir, N° 1263-1). Then, the mixture was centrifuged (Centrifuge Rotoflix 32 A)  
101 at  $3500\times g$  for 10 min and the supernatant was collected, filtered through a Whatman N°4 paper  
102 and evaporated at  $60^\circ\text{C}$  for 72 h until a semi-solid residue was obtained. The extracts were  
103 stored at  $4^\circ\text{C}$  (Labcold, Basingstocke Hants) for analysis.

#### 104 *2.4 Phytochemical analyses of the extracts*

##### 105 *2.4.1 Determination of total polyphenols*

106 The method described by Singleton & Rossi (1965) with slight modifications was used to  
107 determine the total polyphenols' content of the extracts. Briefly, an aliquot of 0.1 mL of extract  
108 (4 mg/mL) was mixed with 0.75 mL of Folin-Ciocalteu reagent (diluted 10 times in distilled  
109 water) and left at room temperature ( $25\pm 1^\circ\text{C}$ ) for 5 min. Then, 0.75 mL of an aqueous solution  
110 of sodium carbonate (6%, w/v) was added. The mixture is stirred using a vortex mixer and  
111 incubated at  $25\pm 1^\circ\text{C}$  in the dark for 90 min. The absorbance of the blue complex formed during  
112 the reaction was read at 725 nm (UVmini-1240, UV-Vis Spectrophotometer, Shimadzu- Japan)  
113 against a blank where the extract was replaced by distilled water. Gallic acid at concentrations  
114 ranging from 0 to 800  $\mu\text{g/mL}$  was used as the standard. The total polyphenols' content of the  
115 different extracts was calculated from the calibration curve ( $r^2=0.97$ ) drawn with standard and  
116 expressed in micrograms of gallic acid equivalent per gram of dry matter ( $\mu\text{g GAE/g DM}$ ).

##### 117 *2.4.2 Determination of flavonoid content*

118 The quantification of total flavonoids was performed following the protocol of Aiyegoro &  
119 Okoh (2010). An aliquot of 0.2 mL of extract (4 mg/mL) was introduced into a tube, followed

120 with the addition of 0.1 mL of aluminum trichloride ( $\text{AlCl}_3$ , 10% w/v), 1 mL of potassium  
121 acetate ( $\text{CH}_3\text{COOK}$ , 1M) and 2.8 mL of distilled water. The mixture was homogenized,  
122 incubated at  $25\pm 1^\circ\text{C}$  for 30 min and the absorbance was read at 415 nm against the blank.  
123 Quercetin at concentrations ranging from 0 to 800  $\mu\text{g}/\text{mL}$  was used as standard. The total  
124 flavonoids' content was calculated from the calibration curve ( $r^2=0.99$ ) and expressed as  
125 micrograms of quercetin equivalent per gram of dry matter ( $\mu\text{g QE}/\text{g DM}$ ).

#### 126 *2.4.3 Determination of alkaloid content*

127 The determination of the alkaloid content was evaluated according to the method of Sing et al.  
128 (2004) with some modifications. In the experimental procedure, 100 mg of the extract was  
129 dissolved in 10 mL ethanol (80%, v/v). The mixture was homogenized and centrifuged at  
130  $5000\times\text{g}$  for 10 min. The bottom was discarded and 1 mL of the supernatant was taken and  
131 introduced into a tube. Then, 1 mL of the mixture [ $\text{FeCl}_3$  (0.025M) + HCl (0.5M)] and 1 mL of  
132 1,10-phenanthroline (0.05M) prepared in ethanol were added. The mixture obtained was  
133 homogenized and incubated for 30 min at  $100^\circ\text{C}$  in a water bath (Poly Science, USA). After  
134 incubation, the absorbance of the red coloration formed was read at 510 nm against the blank.  
135 Quinine at a concentration of 10  $\mu\text{g}/\text{mL}$  was used as the standard and the alkaloid content was  
136 expressed in micrograms of quinine equivalent per gram of dry matter ( $\mu\text{g QuiE}/\text{g DM}$ ).

#### 137 *2.4.4 Determination of vitamin C content*

138 The vitamin C content of the extracts was assessed following the method described by  
139 Mouhannad et al. (2010) with some modifications. Briefly, extracts' solutions at 50 mg/mL  
140 were prepared in distilled water. The solution was diluted with distilled water (50:1 v/v) and 20  
141 mL of the mixture was taken and transferred into an Erlenmeyer of 500 mL followed with  
142 addition of 25 mL of distilled water and 1 mL of starch (0.25 g of soluble starch in 50 mL of  
143 boiling distilled water at  $79^\circ\text{C}$ ). The mixture was titrated with a solution of iodine 0.05 M (2 g  
144 KI and 1.3 g of  $\text{I}_2$ , in 1 L of distilled water) under agitation of a magnetic stirrer (IKA® C-MAG

145 HS 7, Germany) until the formation of a blue-black color that persists for 30 s. The vitamin C  
146 content was expressed in mg of extract per 100 g of dry matter.

## 147 *2.5 Evaluation of antioxidant potential of the extracts*

### 148 *2.5.1 Determination of DPPH (2,2-diphenyl-1-picrylhydrazyl) radical scavenging activity*

149 The DPPH scavenging activity of the extracts from the mangosteen fruit peels was evaluated  
150 using the method described by Sanchez-Moreno et al. (1998). The extracts were prepared at  
151 different concentrations (1.0, 5.0, 10.0, 15.0, and 20.0 mg/mL) and 50  $\mu$ L was mixed with 1.95  
152 mL of a freshly prepared DPPH methanolic solution (0.025 g/L). After 30 min of incubation at  
153  $25\pm 1^\circ\text{C}$  in the dark, the absorbance was read at 515 nm. Methanol was used as a negative control  
154 while ascorbic acid (vitamin C) was used as a positive control. The controls were prepared as  
155 for the test sample where the extract solution was replaced by methanol or ascorbic acid. The  
156 absorbance of the solution was read at 515 nm against the blank. The percentage of inhibition  
157 of the DPPH radical was calculated using the following formula:

$$158 \quad \text{DPPH inhibition}_{(\%)} = \left( \frac{OD_{control} - OD_{sample}}{OD_{control}} \right) \times 100$$

159 The  $\text{IC}_{50}$  value corresponding to the concentration of antioxidants necessary for scavenging  
160 50% of DPPH radical, was calculated from the graph of the DPPH inhibition percentage as a  
161 function of the concentrations of extracts. As the  $\text{IC}_{50}$  value of an extract is low, that extract is  
162 considered as active.

### 163 *2.5.2 Determination of the Ferric Reducing Antioxidant Power (FRAP)*

164 The reducing power of the extracts was determined by the method of Oyaizu (1986). In the  
165 protocol, solutions of extracts at 0.25, 0.50, 0.75 and 1.0 mg/mL were prepared. An aliquot of  
166 1 mL of the extract was mixed with 2.5 mL of phosphate buffer solution 0.2M (pH 6.6) and 2.5  
167 mL of potassium ferricyanide solution ( $\text{K}_3\text{Fe}(\text{CN})_6$  6.1%, w/v). The mixture was incubated in a

168 water bath at 50°C (Poly Science, USA) for 20 min. Then, 2.5 mL of trichloroacetic acid  
169 solution 10% (w/v) were added to the mixture to stop the reaction and the tubes were  
170 centrifuged at 3000×g for 10 min. 2.5 mL of the supernatant was mixed with 2.5 mL of distilled  
171 water and 0.5 mL of ferric chloride solution (FeCl<sub>3</sub>, 0.1%). The absorbance of the mixture was  
172 read at 700 nm against the blank. Distilled water and ascorbic acid (0.25 µg/mL) treated under  
173 the same conditions as the samples were used as positive and negative controls, respectively.  
174 The iron reduction capacity (Fe<sup>3+</sup>) was expressed in µg of ascorbic acid equivalent per gram of  
175 dry matter (µg AAE/g DM).

### 176 *2.5.3 Determination of the Total Antioxidant Capacity*

177 The total antioxidant capacity (TAC) of the extracts was evaluated using the  
178 phosphomolybdenum method described by Prieto et al. (1999). An aliquot of 0.2 mL of extract  
179 at different concentrations (0.50, 0.625, 0.75, 0.875, and 1.00 mg/mL) was mixed with 2 mL of  
180 reactive solution (sulfuric acid 0.6 M, sodium dihydrogenophosphate 28 mM, and ammonium  
181 molybdate 4 mM). The tubes were plugged and incubated at 95°C for 90 min in a water bath.  
182 After incubation, the tubes were cooled and the absorbance was read at 695 nm against the  
183 blank (3 mL of reagent solution and 0.3 mL of methanol). The TAC of the extracts was  
184 calculated using the calibration curve generated with ascorbic acid at concentrations ranging  
185 from 0.01–0.5 mg/mL ( $r^2=0.988$ ) and expressed in milligrams of ascorbic acid equivalent per  
186 gram of dry matter (mg AAE/g DM).

### 187 *2.6 Statistical analyses*

188 All experiments were repeated three times and the results were expressed as a mean ± standard  
189 deviation. The mean values of responses obtained from the two extracts were compared using  
190 the Student t-test and statistical significance was set at  $p<0.05$ . Pearson's correlation was  
191 performed to assess the relationship the bioactive compounds of extracts and the antioxidant

192 activities. All tests were done using the Statistical Package for Social Sciences (SPSS) version  
193 20.0.

### 194 **3 RESULTS**

#### 195 *3.1 Bioactive compounds of different extracts*

196 The bioactive compounds of the different extracts were quantified and the results are presented  
197 in Table 1. The mangosteen fruit peels contained polyphenols, flavonoids, alkaloids and vitamin  
198 C at concentrations which vary significantly ( $p < 0.05$ ) with the extraction solvent. Generally,  
199 ethanol 70% extracted more polyphenols ( $57.19 \pm 0.46$  mg EAG/g DM vs  $27.07 \pm 0.57$  mg EAG/g  
200 DM obtained with distilled water as solvent), flavonoids ( $35.06 \pm 1.46$  mg EQ/g DM vs  
201  $2.01 \pm 0.48$  mg EQ/g DM obtained with distilled water as solvent), alkaloids ( $4.49 \pm 0.00$  mg  
202 EQui/g DM vs  $3.35 \pm 0.03$  mg EQui/g DM obtained with distilled water as solvent) as well as  
203 vitamin C for which  $1.42 \pm 0.01$  mg/100g DM was obtained compared to  $0.55 \pm 0.01$  mg/100g  
204 DM recorded with distilled water (Table 1).

#### 205 *3.2 Antioxidant activities of mangosteen fruit peels' extracts*

##### 206 *3.2.1 Capacity to scavenge DPPH radicals*

207 The ability of extracts from mangosteen fruit peels to scavenge the DPPH radicals is depicted  
208 in Figure 1. Independent of solvent used, the extracts were active in a concentration dependent  
209 manner. While considering the extraction solvent, the hydroethanolic extract was significantly  
210 more active than the aqueous one. The maximum inhibition percentage of DPPH radicals  
211 (85.98%) was obtained with 5 mg/mL of the hydroethanolic extract, while with the aqueous  
212 extract, it was obtained with 20 mg/mL (83.50%). The extract concentration that inhibits 50%  
213 of the DPPH free radicals was calculated and the results obtained showed that the  
214 hydroethanolic extract has an  $IC_{50}$  of 0.29 mg/mL while the aqueous one has an  $IC_{50}$  of 1.05  
215 mg/mL. Although the ethanolic extract was significantly ( $p < 0.05$ ) more active as it showed the

216 lowest IC<sub>50</sub> value, both of the two extracts were less active than the vitamin C used as control  
217 for which an IC<sub>50</sub> value of 3.92 µg/mL was recorded.

### 218 3.2.2 Iron reducing power

219 As observed in Fig. 2, all the extracts showed ability to reduce iron. The reducing power was  
220 proportional to extracts' concentration and the highest reducing power was noticed at the extract  
221 concentration of 1 mg/mL. Considering the effect of extraction solvent, an opposite observation  
222 was made. Aqueous extract with a reducing power of 48.99 mg EAA/g DM was significantly  
223 ( $p<0.05$ ) more active compared to hydroethanolic extract for which a reducing power of 24.77  
224 mg EAA/g DM was obtained.

### 225 3.2.3 Total antioxidant capacity

226 The total antioxidant capacity of the extracts increases as the extraction concentration increases  
227 (Fig. 3). The maximum total antioxidant capacity (0.53 mg EAA/g DM for the hydroethanolic  
228 extract and 0.19 mg EAA/g DM for the aqueous extract) was reached at the extracts'  
229 concentration of 1 mg/mL. Generally, the hydroethanolic extract showed a total antioxidant  
230 capacity significantly ( $p<0.05$ ) higher than the aqueous extract independently of the tested  
231 concentrations.

### 232 3.3 Correlation between the bioactive compounds and the antioxidant activities of extracts

233 Regarding the aqueous extract of mangosteen fruit peels, only alkaloids were positively ( $r^2=1.0$ )  
234 and significantly ( $p<0.05$ ) correlated with scavenging activity. Although non-significant  
235 ( $p>0.05$ ), the total antioxidant capacity was negatively correlated with vitamin C ( $r^2=-0.09$ ),  
236 flavonoids ( $r^2=-0.58$ ), total phenolics ( $r^2=-0.09$ ) and alkaloids ( $r^2=-0.91$ ). The scavenging  
237 activity was positively correlated with total phenolics ( $r^2=0.50$ ), flavonoids ( $r^2=0.86$ ), and  
238 vitamin C ( $r^2=0.50$ ). The reducing power was negatively correlated with total phenolics ( $r^2=-$

239 0.22) and vitamin C ( $r^2=-0.22$ ), but positively correlated with flavonoids ( $r^2=0.29$ ) and alkaloids  
240 ( $r^2=0.73$ ).

241 Considering the hydroethanolic extract of mangosteen fruit peels, no significant ( $p>0.05$ )  
242 correlations were recorded. Vitamin C, flavonoids and total phenolics were negatively  
243 correlated with total antioxidant capacity with  $r^2$  of -0.50, -0.56, and -0.50, respectively. Only  
244 alkaloids were positively correlated with total antioxidant capacity ( $r^2=0.32$ ). Negative  
245 correlations were obtained between the reducing power and alkaloids ( $r^2=-0.32$ ) and flavonoids  
246 ( $r^2=-0.95$ ), and also between the scavenging activity and alkaloids ( $r^2=-0.32$ ). However, the  
247 reducing power was positively correlated to total phenolics ( $r^2=0.12$ ) and vitamin C ( $r^2=0.12$ ).  
248 Positive correlations with  $r^2$  of 0.5, 0.56, and 0.50 were obtained between the scavenging  
249 activity and the total phenolics, flavonoids and vitamin C, respectively.

#### 250 **4 DISCUSSION**

251 Fruit peels are generally considered as wastes and are usually drawn in nature, leading to an  
252 environmental pollution. In this study, we have decided to valorize the mangosteen fruit peels  
253 as functional ingredients that might be used in the food industry for food preservation purpose  
254 or in the medical field for the management and/or prevention of cardiometabolic diseases. For  
255 that, the peels of mangosteen fruits were powdered and bioactive compounds were extracted  
256 using two solvents: distilled water and ethanol: distilled water 70% (v/v). The results obtained  
257 in this study showed that, the mangosteen fruit peels contains bioactive secondary metabolites  
258 such as polyphenols (27.07 - 57.19 mg EAG/g DM), flavonoids (2.01 - 35.06 mg EQ/g DM),  
259 and alkaloids (3.35 - 4.49 mg EQui/g DM) as well as the micronutrient vitamin C (0.55 - 1.42  
260 mg/100g DM). Generally, the highest contents in bioactive compounds (polyphenols,  
261 flavonoids, alkaloids, vitamin C) were noticed in hydroethanolic extract. This could arise from  
262 the polarity of the hydroethanolic solvent. Indeed, ethanol is an organic solvent that can easily  
263 pass through the cell walls and membranes thus facilitating the extraction of a large amount of

264 low polar compounds. It was reported in the literature that biological active compounds present  
265 in plant materials such as alkaloids, tannins, terpenoids, flavonoids and phenolic compounds  
266 are insoluble secondary metabolites (Edoun et al., 2020; Mouafo et al., 2021). Dibacto et al.  
267 (2021) also reported that ethanol 70% extracted more polyphenols and flavonoids compared to  
268 distilled water. Moreover, the presence of distilled water at 30% in that solvent might also  
269 enable the extraction of some water soluble bioactive compounds, leading to an increase in their  
270 contents. Indeed, addition of water to organic solvent increases the solubility of compounds by  
271 modulating their polarity through a weakening of hydrogen bonds (Albano & Miguel, 2010).

272 The total polyphenols content of the hydroethanolic extract obtained in this study (57.19 mg  
273 EAG/g DM) was higher than that reported by González et al. (2019) ethanolic extract of  
274 *Passiflora edulis* peels, a fruit that the peel has the same sticky structure like mangosteen fruit.

275 They found a total polyphenols content of  $37.70 \pm 0.13$  mg EQ/g of extract. However, opposite  
276 observation was noticed regarding flavonoids as the value reported by these authors  
277 ( $55.60 \pm 0.11$  mg EQ/g) was higher than that obtained in this study (35.06 mg EQ/g DM).

278 Regarding the aqueous extract of mangosteen fruit peels, their polyphenols and flavonoids  
279 contents were higher than that reported by Ramli et al. (2020) with aqueous extract of *P. edulis*  
280 peels (total polyphenols of  $7.273 \pm 0.002$  mg EGA/g and flavonoids of  $8.364 \pm 0.002$  mg EQ/g).

281 This could be ascribed to the composition of peel which varies from a fruit to another. The high  
282 content of polyphenols and flavonoids (which are bioactive compounds endowed with  
283 biological activity) in the mangosteen fruit peel suggests the potential use of these wastes as  
284 functional ingredients. Besides these bioactive secondary metabolites, the presence of vitamin  
285 C in these peels suggests their potential use as a novel and green foods preservative ingredient.

286 To strengthen these hypotheses, the antioxidant activity of the extracts was assessed. Three  
287 methods were used as extract constituents might act through different mechanisms. They were  
288 the free radicals scavenging activity, the iron reducing power and the total antioxidant capacity.

289 One of the most widely used, easiest and efficient method to assess the antioxidant activity of  
290 a compound is the scavenging model of DPPH radical. It measures the ability of a compound  
291 to donate hydrogen radicals to scavenge DPPH radicals (Surveswaran et al., 2007). In this study,  
292 all the mangosteen fruit peels extracts were able to scavenge the DPPH radicals and convert it  
293 into species (DPPH-H or DPPH-R) which are a more stable. The greatest inhibition percentage  
294 of the DPPH radicals was recorded with the hydroethanolic extract of mangosteen fruit peels.  
295 This could be attributed to its high contents in total phenolics, flavonoids and vitamin C. In fact,  
296 the presence of hydroxyl groups in the structure polyphenols, flavonoids and vitamin C confers  
297 to these latter a strong ability to give more hydrogen atoms to stabilize free radicals (Torres de  
298 Pinedo et al., 2007). Moreover, the electron donating ability of vitamin C and flavonoids lead  
299 to the conversion of free radicals into a more stable form as reported by Dibacto et al. (2021).  
300 The positive correlations between the scavenging activity of the both extracts and their total  
301 phenolics, flavonoids and vitamin C contents also justify the involvement of these bioactive  
302 compounds in the antioxidant mechanisms. Thus, the presence polyphenols, flavonoids and  
303 vitamin C in mangosteen fruit peels suggests that byproducts as a potential functional food  
304 ingredient useful to fight against the oxidative stress and its consequences like cardiovascular  
305 and neurodegenerative diseases mainly due to the free radicals which attack and cause damage  
306 to our cells.

307 Regarding the aqueous extract of mangosteen fruit peels, only alkaloids were positively ( $r^2=1.0$ )  
308 and significantly ( $p<0.05$ ) correlated with scavenging activity. However, that observation was  
309 no made with hydroethanolic extract despite its highest alkaloids content. This could be  
310 ascribed to the chemical structure of the alkaloids extracted with distilled water and suggests  
311 that further analyses on the alkaloids profile of the aqueous extract of mangosteen fruit peels  
312 should be investigated in order to identify that novel alkaloids endowed with powerful  
313 scavenging activity. Račková et al. (2004) also reported that the scavenging mechanism of

314 alkaloids depends on their chemical structure and increases with their degree of hydroxylation.  
315 Indeed, some alkaloids contain phenolic, OH, OCH<sub>3</sub>, NH<sub>2</sub> and NH functional groups. In  
316 presence of free radicals, they can donate their hydrogen and end the chain reaction with the  
317 formation of the oxidized form of DPPH which is stable (Al-Sehemi & Irfan, 2017).

318 Another antioxidant mechanism of the extracts assessed in this study was their reducing power  
319 through the ferric reducing antioxidant power (FRAP). This method is based on the capacity of  
320 a compound to donate electron leading to the reduction of Fe<sup>3+</sup> into Fe<sup>2+</sup> (Yang & Zhai, 2010;  
321 Rohman et al., 2019). The mangosteen fruit peels independently of the extraction solvent  
322 showed ability to reduce ferric ions in a dose dependent manner. Azima et al. (2014) also  
323 reported that mangosteen fruit peel extracts possessed a good reducing power which is higher  
324 compared to other extracts from fruit peels like guava and *Clitoria ternatea*. In this study, the  
325 reducing power of extracts showed different behavior compared to scavenging activity where  
326 the hydroethanolic extract with the highest content in bioactive compounds was more active. In  
327 fact, aqueous extract exhibited the highest reducing power. This can arise from the chemical  
328 structure of compounds extracted with distilled water as solvent. Kaurinovic & Vustag (2018)  
329 also pointed out the good correlation between the reducing power and the chemical structure of  
330 bioactive compounds rather than their contents. The highest correlation of the reducing power  
331 was recorded in the present study with alkaloids ( $r^2=0.73$ ) from aqueous extract of mangosteen  
332 fruit peels. This can be explained by the chemical structure of alkaloids extracted with distilled  
333 water. In fact, some alkaloids possess in their side chains of isoprene unit a high electron  
334 density. In their ferric reducing power mechanism, they act as electron donor leading to the  
335 purge radical species (Ng et al., 2018). The position and the number of hydroxyl groups in the  
336 chemical structure of the alkaloids also play a critical role in their ferric reducing power  
337 (Abderrahim et al., 2016). The reducing power of extracts from mangosteen fruit peels suggests  
338 their potential use in the medical field to manage and prevent oxidative damage in

339 neurodegenerative disorders including aging, atherosclerosis, cancer, diabetes, Parkinson's and  
340 Alzheimer's diseases which are associated to transition metal ions and formation of reactive  
341 oxygen species. They can substitute of synthetic compounds for which side effects are  
342 continuously reported.

343 With regard to total antioxidant capacity, both extracts were active in reducing Molybdate (VI)  
344 to Molybdate (V) in a dose-dependent manner. This observation can be related to the  
345 exponential development of the reduction power when the concentration of the extract increases  
346 (Tanaka et al., 1988). The hydroethanolic extract exhibited the highest total antioxidant capacity  
347 (0.53 mg EAA/g DM) compared to aqueous extracts. Notwithstanding that observation, it is  
348 noteworthy to note that in aqueous extract, the total antioxidant capacity was negatively  
349 correlated with total phenolics ( $r^2=-0.09$ ), flavonoids ( $r^2=-0.58$ ), vitamin C ( $r^2=-0.09$ ) and  
350 alkaloids ( $r^2=-0.91$ ). While in hydroethanolic extract, a positive correlation was made only  
351 between the total antioxidant capacity and alkaloids ( $r^2=0.32$ ). This suggests that either  
352 alkaloids or other non-identified compounds of the extracts such as tannins, saponins,  
353 polysaccharides, and anthocyanins might be responsible of the total antioxidant capacity  
354 assessed through the reduction of molybdate (VI) to molybdate (V). These results corroborate  
355 those of Kadum et al. (2019) and Farahmandfar et al. (2019) who showed that the total  
356 antioxidant capacity is often dependent on the presence of some alkaloids and polyphenols  
357 rather than the quantity of flavonoids and others.

358 This study is the first of its kind relating to evaluate the bioactive compounds and antioxidant  
359 potential of mangosteen fruit grown in Cameroon. Perhaps the main limitation of this study is  
360 the fact that an *in vivo* study in rats were not conducted. In fact, an in-depth study on toxicity  
361 and metabolic disorders in rats of mangosteen fruit peels will allow the valorization of this  
362 waste.

363

**364 5 CONCLUSIONS**

365 This study indicates that bioactive compounds with different features can be extracted from  
366 mangosteen fruit peels using distilled water and ethanol 70% as extraction solvents. In addition,  
367 mangosteen fruit peels is a good and natural source of vitamin C, phenolic compounds,  
368 flavonoids and alkaloids. The aqueous and hydroethanolic extracts from these peels displayed  
369 free radicals scavenging activity and iron reducing power. They also demonstrated excellent  
370 total antioxidant capacity thus suggesting their use as natural antioxidants in substitution of  
371 their chemical counterparts. The present study also suggests that in spite of chemical products  
372 which are already available on markets, natural alternatives should be considered in the  
373 governmental measures for food preservation as well as the prevention and management of  
374 metabolic diseases.

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499 **List of Tables**

500

501 TABLE 1 Contents in total phenolics, flavonoids, alkaloids and vitamin C of extracts from

502 mangosteen fruit peels

503

Extracts	Bioactive compounds			
	Total Phenolic (mg GAE/g DM)	Flavonoids (mg QE/g DM)	Alkaloids (mg QiE/g DM)	Vitamin C (mg/100g DM)
AE	27.07±0.57 <sup>a</sup>	2.01±0.48 <sup>a</sup>	3.35±0.03 <sup>a</sup>	0.55±0.01 <sup>a</sup>
HE	57.19±0.46 <sup>b</sup>	35.06±1.46 <sup>b</sup>	4.49±0.00 <sup>b</sup>	1.42±0.01 <sup>b</sup>

504 AE=Aqueous Extract; HE=Hydroethanolic Extract; Values bearing different superscript letters in the same column

505 are significantly different at p&lt;0.05.

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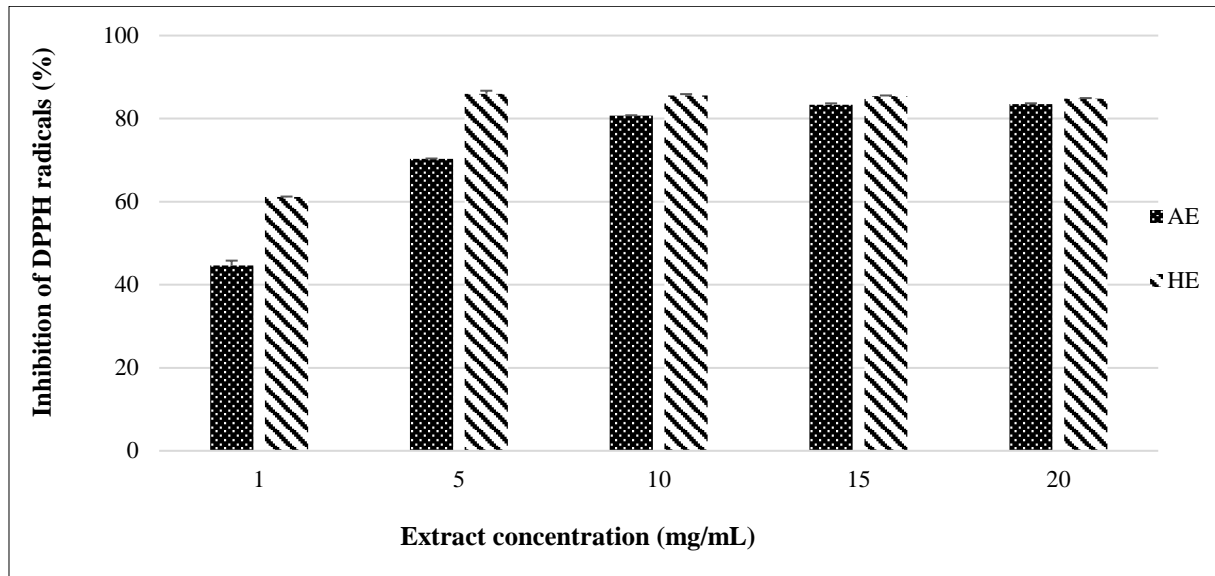
507 TABLE 2 Correlation between bioactive compounds of different extracts from mangosteen fruit peels and antioxidant activities

Extracts	Antioxidant tests	Alkaloids	Total Phenolic	Flavonoids	Vitamin C
Aqueous extract	TAC	$r^2=-0.910$ ; $p=0.272$	$r^2=-0.096$ ; $p=0.939$	$r^2=-0.581$ ; $p=0.606$	$r^2=-0.096$ ; $p=0.939$
	FRAP	$r^2=0.731$ ; $p=0.478$	$r^2=-0.225$ ; $p=0.856$	$r^2=0.292$ ; $p=0.811$	$r^2=-0.225$ ; $p=0.856$
	DPPH	$r^2=1.00$ ; $p=0.000^*$	$r^2=0.500$ ; $p=0.667$	$r^2=0.866$ ; $p=0.333$	$r^2=0.500$ ; $p=0.667$
Hydroethanolic extract	TAC	$r^2=0.327$ ; $p=0.788$	$r^2=-0.500$ ; $p=0.667$	$r^2=-0.569$ ; $p=0.614$	$r^2=-0.500$ ; $p=0.667$
	FRAP	$r^2=-0.308$ ; $p=0.801$	$r^2=0.123$ ; $p=0.922$	$r^2=-0.950$ ; $p=0.203$	$r^2=0.123$ ; $p=0.922$
	DPPH	$r^2=-0.327$ ; $p=0.788$	$r^2=0.500$ ; $p=0.667$	$r^2=0.569$ ; $p=0.614$	$r^2=0.500$ ; $p=0.667$

508  $r^2$ =Correlation coefficient;  $p$ =P-value. DPPH=2, 2-diphenyl-1 picrylhydrazyl; FRAP=ferric reducing antioxidant power; TAC=total antioxidant capacity. \*indicates a significant  
509 at  $p<0.05$ .

510 **List of Figures**

511



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513 **FIGURE 1** Inhibition percentage of DPPH radicals of the aqueous and hydroethanolic extracts  
514 from mangosteen fruit peels.

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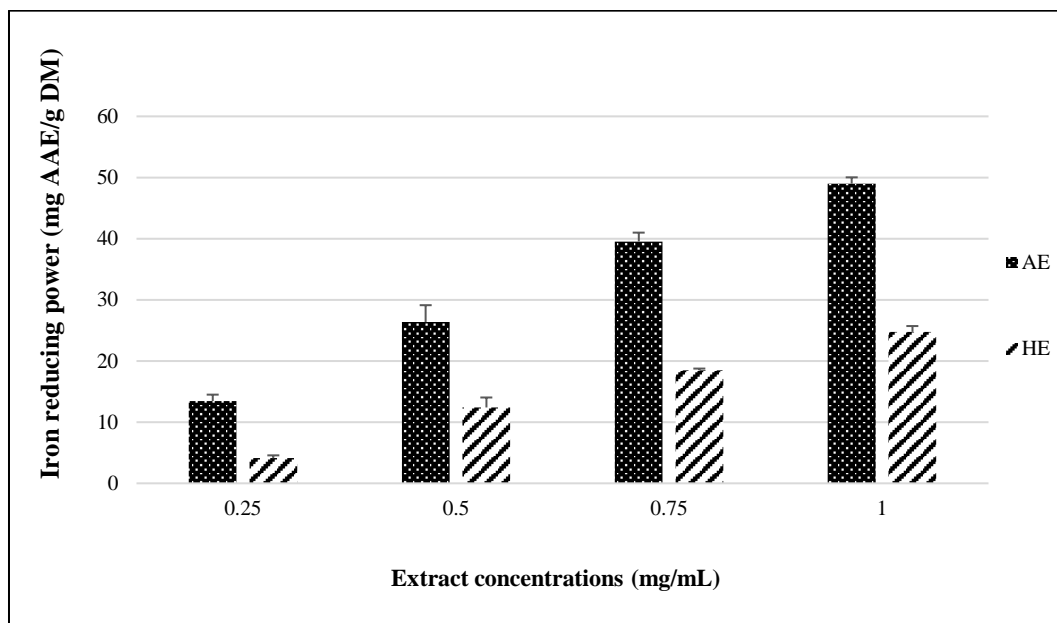
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525 FIGURE 2 Iron reducing power of the aqueous and hydroethanolic extracts of mangosteen fruit  
526 peels.

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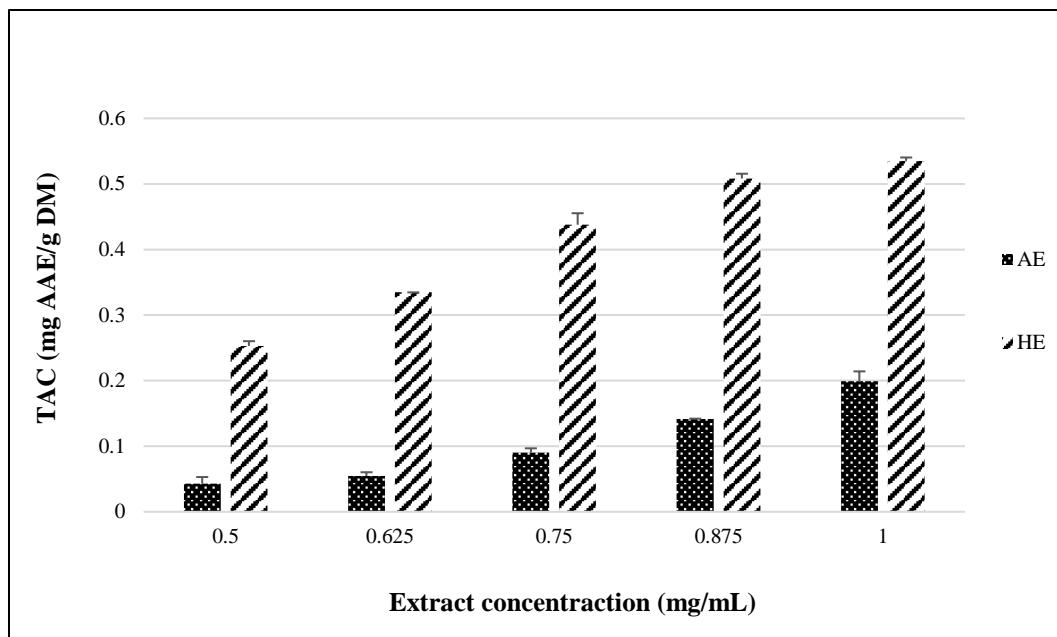
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537 FIGURE 3 Total antioxidant capacity of the aqueous and hydroethanolic extracts of mangosteen  
 538 fruit peels.

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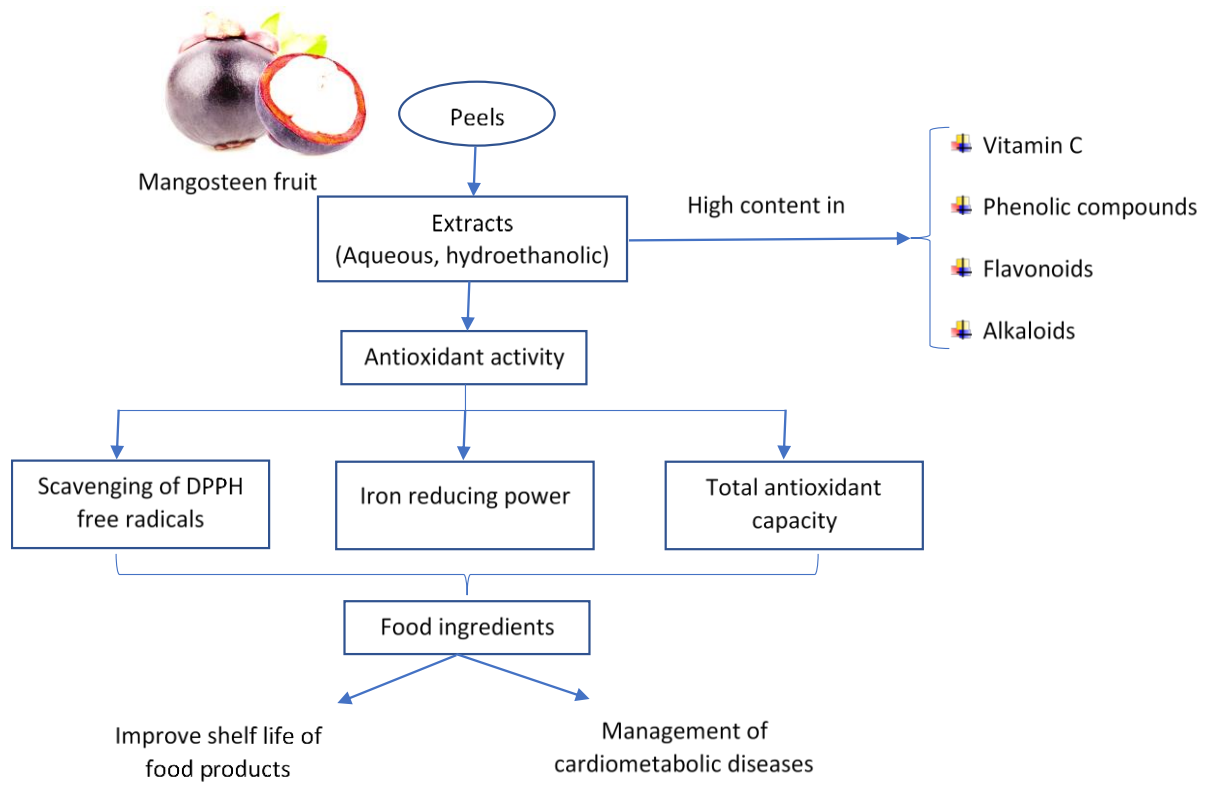
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550 FIGURE 4 Graphical abstract.