Chapter 5

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Abstract

The bark of Mimosa tenuiflora is a traditional remedy for several skin ailments like burns, ulcer and psoriasis and plays furthermore a role in the treatment of wounds. For ethnopharmaceutical use the bark is usually powdered and often applied as decoct or cataplasm. According to the studies performed with Mimosa tenuiflora to the present, it seems that the wound-healing activity of this plant is due to a combination of the several different compounds (tannins and flavonoid mainly). In this chapter, the structure of the tannin and flavonoid was analyzed by PM3 and AM1 methods since represent the main constituents of the Mimosa tenuiflora. It is determined by the electrostatic potential and the molecular orbitals that the hydroxyl group of the flavonoid structure it is attracted by the oxygen present in the carbonyl group of the structure of tannins. In addition to the main signals of FTIR analyses.

Keywords: Mimosa Tenuiflora, PM3, AM1

5.1 Introduction

Mimosa hostilis is the former scientific name for *Mimosa tenuiflora*, and the two names are synonymous [1-2]. The older name is still widely know due to its presence in the literature and as distributers of botanical products still use the older term. *M. tenuiflora* is an entheogen known as *Jurema, Jurema Preta,* *Black Jurema*, and *Vinho de Jurema*. Dried Mexican *Mimosa Hostilis* root bark has been recently shown to have a DMT content of about 1%. The stem bark has about 0.03% DMT (Figure 5.1).

Figure 5.1 *Mimosa tenuiflora.*

To date no β-carbolines such as harmala alkaloids have been detected in *Mimosa tenuiflora* decoctions, however the isolation of a new compound called "Yuremamine" from *Mimosa tenuiflora* as reported in 2005 represents a new class of phyto-indoles [3]. This may explain the reported oral activity of DMT in Jurema without the addition of an MAOI. Imported MHRB typically requires the addition of an MAOI in the preparation of ayahuasca.

In Mexico in 1984, this natural resource was utilized empirically to alleviate the sufferings of hundreds of victims of large natural-gas depot explosion; on that occasion, direct application of powdered *Mimosa tenuiflora* bark on patients' burns resulted in facilitation of skin regeneration and prevention of scarring in many of the patients. Subsequently, news of the existence of a miraculous Mexican tree skin was spread worldwide by the mass media, producing a rise in spotlighting commercial attention on this natural product and included the elaboration of several products with supposed medicinal properties.

During the 1990s pharmacological and phytochemical studies performed by Mexican research groups supported the existence of natural compounds with cicatrizing properties in *Mimosa tenuiflora* cortex. A series of pre-clinical experimental studies concluded that water and alcoholic extracts obtained from the dried bark of *Mimosa tenuiflora* are particularly rich in tannins and that these also contain steroidal saponins biological activity of these extracts was defined as (a) possessing strong *in vitro* antimicrobial properties against a wide group of microorganisms, yeasts, and dermatophytes and (b) inducing the growth *in vitro* of fibroblasts and other human cells [4].

5.2 Secondary Metabolites of *Mimosa Tenuiflora*

The phytochemistry of *M. tenuiflora* has attracted considerable interest, mainly due to the presence of indole alkaloids and tannins (proanthocyanidins). However, phytochemical reports on others classes of the compounds that may be present are rare.

- **Alkaloids**

Two indole alkaloids have been isolated from "jurema": 5-hydroxy-tryptamine, and N, N-dimetyltryptamine. The latter is also found in the root bark, and is linked to its hallucinogen use, as mentioned above. The alkaloid N, N-dimetyltryptamine was apparently detected for the first time by Gonçalves de Lima and his team, after a visit to the Pancararu village in Brejo dos Padres (Pernambuco state, northeastern Brazil). The substance isolated was called nigerine. Ott (2002), however, suggested that this product could be an impure form of N, N-dimetyltryptamine. Vepsäläinen et al. (2005) performed one phytochemical study of this species with advanced instrumentation and methodologies, particularly ^{1}H-^{13}C nuclear magnetic resonance (NMR) and liquid chromatography-mass spectrometry (LC-MS) under mild acidic pH. A new phytoindole, Yuremamine, was isolated from the stem bark of *M. tenuiflora* in this study (Figure 5.2).

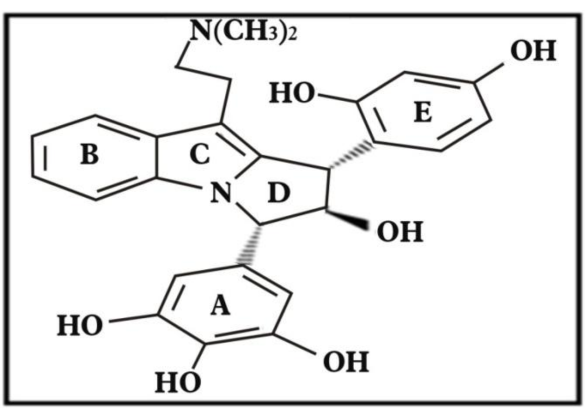

Figure 5.2 *Yuremamine from the stem bark of Mimosa tenuiflora.*

- **Chalcones**

Other studies demonstrated the presence of two chalcones: kukulkan A (2',4'-dihydroxy-3',4-dimetoxychalcone); and kukulkan B (2',4',4-trihydroxy-3'-metoxychalcone)((Figure 5.3).

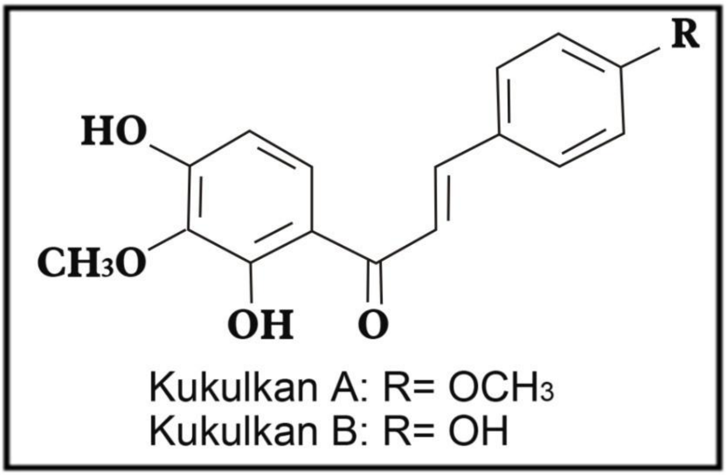

Figure 5.3 *Chalcones isolated from the stem bark of Mimosa tenuiflora.*

- **Steroids and Terpenoids**

Among the several substances three steroids were isolated from the stem bark of *M. tenuiflora*: campesterol-3-O-beta-D-glucopyranosyl, stigmasterol-3-O-beta-D-glucopyranosyl, and beta-sitosterol-3-O-beta-D-glucopyranosyl. Three saponins have also been identified: mimonoside A, mimonoside B, and mimonoside C (Figure 5.4). Anton et al recorded the presence of the triterpenoid lupeol.

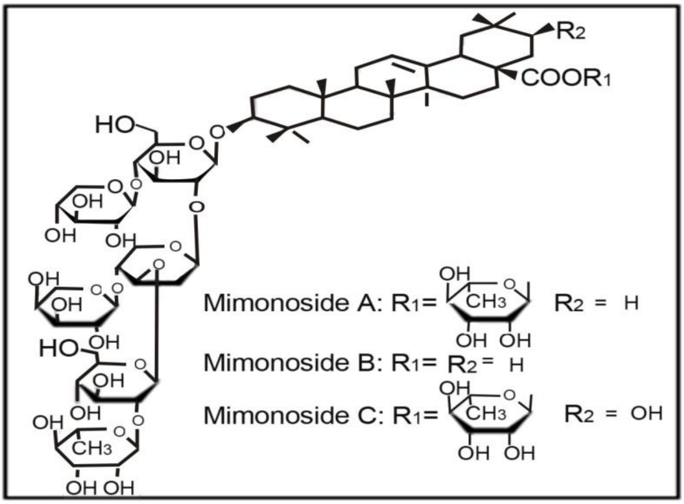

Figure 5.4 *Triterpenoids saponins isolated from the stem bark of Mimosa tenuiflora.*

- **Phenoxychromones**

Five 2-phenoxychromones ("uncommon" flavonoids), the tenuiflorin A [5, 7-dihydroxy-2-(3-hydroxy-4-methoxyphenoxy)-6 methoxychromone], tenuiflorin B [5, 7-dihydroxy-2- (4-hydroxy-3-methoxyphenoxy)-6-methoxychromone] and tenuiflorin C [5,7-dihydroxy-2-(3-hydroxy-4-methoxyphenoxy)-chromone], along with 6-demethoxycapillarisin and 6-demethoxy-4'-O-methylcapillarisin were isolated from the leaves of *M. tenuiflora* (Figure 5.5). These uncommon "flavonoids" exhibited an unusual ether linkage between the B and C ring.

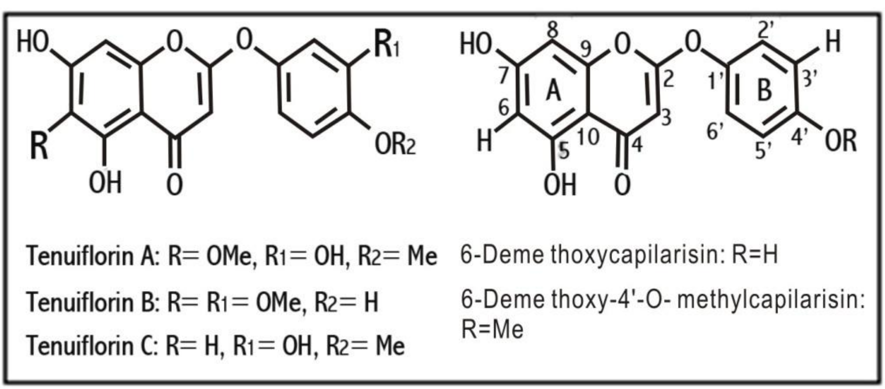

Figure 5.5 *Phenoxychromones isolated from the leaves of Mimosa tenuiflora.*

- Pharmacological Studies of the Extracts

1) Antimicrobial activity

Tables 5.1 and 5.2 show results of the experiments undertaken to test for any antimicrobial activity of the substances from the bark of *M. tenuiflora*. Tannins are probably responsible for most of this activity. An ethanol extract (95 %) was active against *Micrococcus luteus* and *Bacillus subtilis.* Table 5.2 lists the species of the fungi (*Microsporum canis*, *Microsporum gypseum*, *Trichophyton mentagrophytes*, *Trichophyton rubrum*, and *Chaetomium indicum*) against which the activity was observed. The substances extracted with ethanol (95%) were also effective against *Candida albicans*.

Table 5.1 *Antibacterial activity related from Mimosa tenuiflora.*

EXTRACT /ACTIVE DOSE	RESULTS /TESTED MICROORGANISM
Buthanol 5 mg/well	*Staphylococcus aureus*
Buthanol 15 mg/well	*Escherichia coli*
Methanol 5 µg/well	*Staphylococcus aureus*
Methanol 15 µg/well	*Escherichia coli*
Ethyl Acetate 5 mg/well	*Escherichia coli*
Ethyl Acetate 10 mg/well	*Staphylococcus aureus*
Ethanol (95%) MIC > 10 µg/mL	*Staphylococcus epidermidis and Acinetobacter calcoaceticus*
Ethanol (95%) MIC 10 µg/mL	*Staphylococcus aureus Micrococcus luteus*
Ethanol (95%) MIC 20 µg/mL	*Escherichia coli and Klebsiella pneumoniae*
Ethanol (95%) MIC 40 µg/mL	*Pseudomonas aeruginosa*
Ethanol (95%) 5 µg/disc	*Escherichia coli*
Ethanol (95%) 5 µg/disc	*Bacillus subtilis*
Ethanol (95%) 5 µg/disc	*Micrococcus luteus*

Table 5.2 *Antifungical activity related from Mimosa tenuiflora.*

EXTRACT / ACTIVE DOSE	RESULTS / TESTED MICROORGANISM
Ethanol (95%) MIC 10 μg/mL	*Microsporum canis, Microsporum gypseum, Trichophyton mentagrophytes, Trichophyton rubrum and Chaetomium indicum*
Ethanol (95%) 10 μg/mL	*Penicillium oxalicum*
Ethyl acetate 30 mg/well	*Candida albicans*
Ethanol (95%) MIC 70 μg/mL	*Candida albicans*

2) Antiinflammatory and healing action

Tellez and Dupoy de Guitard demonstrated the effectiveness of *Mimosa tenuiflora* in the topical treatment of the eczema (10% concentration), as well as against the inflammations (as a powder made from the dry bark) in the humans. In a similar experiment, the use of the dry bark of *Mimosa tenuiflora* proved to be effective in wound healing and in the treatment of venous leg ulceration disease.

3) Antispasmolytic action

Meckes-Lozoya et al., using a spray of the bark extract, observed (Table 5.3), the inhibition of the intestinal peristalsis due to a relaxation of the ileum smooth muscle tissue; an increase in the muscular tonus and in the frequency of the contractions of the uterus segments; and an increase in the muscular tonus of the stomach walls. All these experiments were performed with the rats and guinea pigs.

The butanol extract was the most efficient, and contained the most alkaloids. A fraction containing the indolalkylamine and three other smaller bases were responsible for inhibiting the peristaltic reflex of the intestine, resulting in the relaxation of the ileum observed in the guinea pigs.

4) Hemolytic activity

Mekces-Lozoya et al. reported the hemolytic activity of the raw extracts of the stem bark (Table 5.3). Triterpenic saponines, the substances considered responsible for this activity, cause membrane rupture in the erythrocytes. Studies undertaken in 1992 detected a hemolytic effect in low concentrations of a methanol extract containing alkaloids, and a haemagglutinant effect in high doses [5].

Table 5.3 *Biological activities from crude extracts of Mimosa tenuiflora (wild) poir.*

ACTIVITY	TESTED IN	EXTRACT / CONCENTRATION	RESULT
Hemolytic	Erythrocytes	Buthanol 250 µg/mL	74% of hemolyse
		Ethyl acetate 250 µg/mL	48% of hemolyse
		Methanol 500 µg/mL	68% of hemolyse
Wound healing	Adult human external use	10%	Active
		Not related (powder)	Active
Alteration in muscular tonus	Guinea pig and mouse (all the tests)	Buthanol 30 µg/mL	Increase of muscular tonus and the frequency of contraction of the uterus. Active in stomach (increase muscular tonus in rats and relaxation in guinea pig) and ileum (relaxation)
		Ethyl acetate 30 µg/mL	
		Methanol 30 µg/mL	
	Guinea pig	Alkaloid crude fraction 100 µg/mL	Inhibition of the peristaltic reflex (ileum)
		Alkaloid crude fraction 25 µg /mL and 35 µg/mL	

5.3 Results and Discussions of Simulations Analyses

5.3.1 Optimization Energy

Table 5.4 shows the Gibbs energy free of *Mimosa tenuiflora* using PM3 and AM1 methods. In this table can be observed that the negatives values of *Mimosa tenuiflora* are energetically favorable. Figure 5.6 shows that the hydroxyl group (17-27 bond) of the flavonoid structure it is attracted by the oxygen present in the C=O bond (carbonyl group) of the structure of tannin (7-10 bond), because of attractions by hydrogen bonds. Is important mention that with both methods the obtained geometry (ΔG) is appropriate to carry out a reaction, however applying the PM3 method gets a major attraction due to the equation of this method.

These interactions play important roles in the chemical reaction. So, the *Mimosa tenuiflora* bark got into strong focus of modern scientific investigation of skin treatment [6].

Table 5.4 *Gibbs energy free for Mimosa tenuiflora structure.*

Method	ΔG (Kcal/mol)
AM1	- 6005
PM3	- 6372

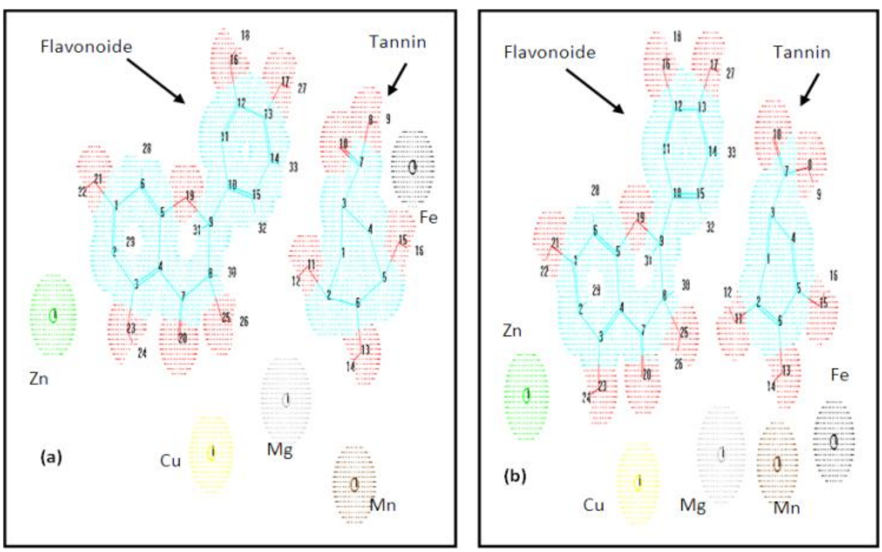

Figure 5.6 *Geometry optimization (ΔG) of Mimosa tenuiflora, where (a) PM3 and (b) AM1 method.*

5.3.2 Structural Parameters

The results of structural parameters of the structure of the tannin and flavonoid main constituents of *Mimosa tenuiflora*, through the application of PM3 and AM1 semi-empiric methods, are shown in Tables 5.5 and 5.6 respectively. These results in conjunction with Figure 5.6 indicate that both structures are not linear. It fact, the large quantity of hydroxyl groups (Figure 5.6) of the flavonoids makes them highly reactive, providing numerous focal points capable of forming hydrogen bonds being the reason why form reversible associations with the flavonoids of *Mimosa tenuiflora* [7].

Table 5.5 *Structural parameters of flavonoids structure.*

Bond length (Å)	**PM3**	**AM1**	**Angle (Å)**	**PM3**	**AM1**
1-2	1.36	1.33	1-2-3	124.12	122.34
2-3	1.52	1.48	2-3-4	120.22	118.98
3-4	1.41	1.34	3-4-5	115.34	113.72
4-5	1.60	1.55	4-5-6	123.97	122.90
5-6	1.37	1.31	5-6-1	117.46	116.35
6-1	1.57	1.46	1-21-22	120.48	119.65
1-21	1.35	1.33	1-2-29	63.870	62.280
21-22	0.96	0.84	1-6-28	121.23	120.83
2-29	0.82	0.75	2-3-29	60.250	60.000
3-23	1.36	1.22	2-3-23	112.50	111.34
23-24	0.95	0.90	3-23-24	124.55	123.05
6-28	1.05	1.00	4-3-23-24	0	0
4-5	1.60	1.55	5-6-28	121.29	120.84
5-19	1.45	1.38	3-4-7	124.16	123.75
4-7	1.54	1.49	4-7-20	117.91	116.39
7-8	1.62	1.53	4-5-19	115.13	114.42
8-9	1.52	1.46	4-7-8	120.20	118.69
9-19	1.50	1.37	7-8-9	116.06	114.83
9-31	0.91	0.83	8-9-19	120.56	118.91
7-20	1.23	1.11	9-19-5	127.54	122.75
8-25	1.48	1.32	7-8-20	121.88	118.35
25-26	0.98	0.93	7-8-25	94.950	92.380
8-30	1.06	1.00	8-25-26	127.81	125.69
9-10	1.51	1.49	8-30-25	62.110	60.125
10-11	1.47	1.35	8-9-31	73.330	71.962
11-12	1.34	1.28	9-19-31	47.220	45.371
12-13	1.46	1.39	9-10-11	121.51	119.84
13-14	1.34	1.27	10-11-12	121.59	120.05
14-15	1.46	1.35	11-12-13	119.62	118.46
15-10	1.34	1.28	12-13-14	119.24	117.83
12-16	1.35	1.30	13-14-15	120.60	119.03
16-18	0.96	0.91	14-15-10	120.84	119.56
13-17	1.35	1.33	11-12-16	118.48	117.02
17-27	0.96	0.93	12-16-18	120.98	120.00
14-33	1.05	1.02	12-13-17	120.66	119.34
15-32	1.04	1.00	13-17-27	120.86	112.45

Table 5.6 *Structural parameters of tannin structure.*

Bond length (Å)	PM3	AM1
1-2	1.47	1.40
1-3	1.46	1.38
3-4	1.61	1.49
4-5	1.62	1.55
5-6	1.62	1.52
6-2	1.61	1.48
2-11	1.41	1.33
11-12	0.96	1.00
3-7	1.52	1.47
7-8	1.36	1.26
8-9	0.96	0.99
7-10	1.23	1.18
5-15	1.41	1.37
15-16	0.96	0.99
6-13	1.41	1.40
13-14	0.96	0.99

Angle (Å)	PM3	AM1
1-2-3	149.49	148.8
1-3-4	63.53	63.03
3-4-5	146.58	145.86
4-5-6	89.08	88.90
5-6-2	144.42	144.33
6-2-1	65.86	64.48
1-2-11	82.20	80.05
2-11-12	108.47	107.62
3-7-10	79.44	79.13
3-4-7	80.32	80.00
7-8-10	84.69	83.26
7-8-9	113.12	112.81
4-5-15	66.52	66.01
5-15-16	108.53	108.23
5-6-13	106.37	106.09
6-13-14	110.19	118.45
2-6-13-14	0	0

5.3.3 FTIR Analyses

The FTIR results of *Mimosa tenuiflora* (tannins and flavonoids) is shown in Table 5.7 in where can be appreciated that these results are very similar between PM3 and AM1 methods. At 5697, 5647, 5485, 5102 and 4514 cm^{-1} corresponds to aromatic C-H signals (flavonoids). Between 4932–4912 cm^{-1} is assigned to OH stretching (flavonoid). The sign at 3480 and 3473 cm^{-1} is attributed to C=O and C=C (flavonoid) [8]. At 2790 and 2675 cm^{-1} corresponds to C=C bond (tannins), between 1332 and 1412 cm^{-1} is assigned to OH (tannins). From 375 to 366 cm^{-1} is attributed to OH out of plane (tannins). Finally the sign at 46, 38 and 33 cm^{-1} corresponds to different minerals present in the *Mimosa tenuiflora* [9-10].

Table 5.7 *FTIR results of Mimosa tenuiflora (flavonoids and tannins) attributed to PM3 and AM1 method.*

ASSIGNMENT	PM3 (FREQUENCIES CM^{-1})	AM1 (FREQUENCIES CM^{-1})
CH stretching (flavonoid)	5697, 5102, 4514	5647, 5485
OH stretching (flavonoid)	4912	4932
C=C (flavonoid)	3706, 3484	3684
C=O, C=C (flavonoid)	3480	3473
C=C (tannin)	2790	2675
C-C (flavonoid)	1845, 1613	1841
C-O (flavonoid)	1317	1296
OH (flavonoid and tannin)	1093	1060
OH (tannin)	1412	1332
OH out of plane (tannin)	375	366
Minerals (Zn, Cu, Mn, Mg, Fe)	46, 33	38

5.3.4 Electrostatic Potential

Electrostatic potentials were obtained through the application of the PM3 and AM1 methods, Figure 5.7 shows that the potentials have values of 0.555-0.067 and 1.001-0.70 eV, respectively, Both methods show that the nucleophillic regions (green color) are located in links OH of the flavonoid structure and tannins is due to the numerous phenol groups in the tannin structure. The main reaction of tannins is thought to be between the oxygen of the C=O bond (COOH group) in the tannins and the OH group of the flavonoids [11].

5.3.5 Molecular Orbitals

The results of molecular orbital using PM3 and AM1 methods for *Mimosa tenuiflora* is shows in Tables 5.8 and 5.9. These results are very similar between both methods. HOMO orbitals in flavonoids and the LUMO orbitals in the tannins play an important role in chemical reactivity of *Mimosa tenuiflora.* The results showed that, in consideration of the atomic charges and the distribution of HOMO, A-ring of the flavonoid structure is the nucleophilic center [12]. This is due to that the tannins are amphipathic molecules having both hydrophobic aromatic rings and hydrophilic hydroxyl groups. These two properties allow tannins to simultaneously bind at several sites on the surface of other molecules [13].

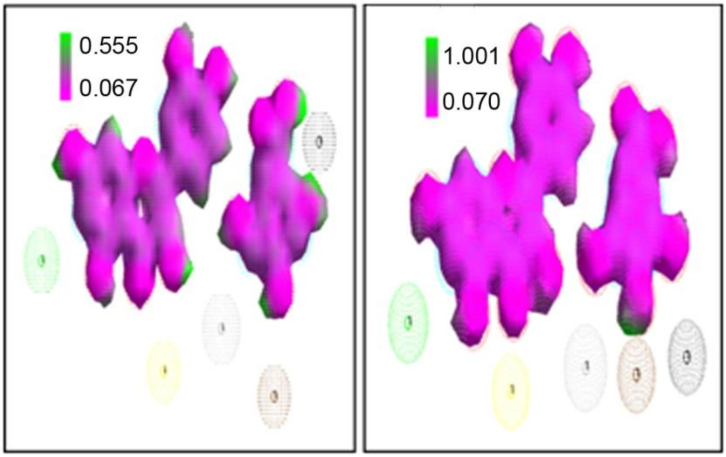

Figure 5.7 *Electrostatic potential of Mimosa tenuiflora (flavonoids and tannins) using (a) PM3 and (b) AM1 method.*

Table 5.8 *HOMO and LUMO orbitals for Mimosa tenuiflora (tannins and flavonoids) using PM3 method.*

ORBITAL	HOMO		LUMO	
	ENERGY (eV)	SYMMETRY (Å)	ENERGY (eV)	SYMMETRY (Å)
50	-16.72	0	3.814	0
20	-12-26	0	1.512	0
10	-11.41	0	0.192	0
5	-10.38	0	-0.750	0
-5	-0.747	0	-10.28	0
-10	0.199	0	-11.31	0
-20	1.516	0	-12.17	0
-50	3.814	0	-16.69	0

Table 5.9 *HOMO and LUMO orbitals for Mimosa tenuiflora (tannins and flavonoids) using AM1 method.*

ORBITAL	HOMO		LUMO	
	ENERGY (eV)	SYMMETRY (Å)	ENERGY (eV)	SYMMETRY (Å)
50	-16.79	0	3.53	0
20	-14.07	0	1.21	0
10	-11.56	0	-0.23	0
5	-10.37	0	-0.970	0
-5	-1.00	0	-10.29	0
-10	-0.22	0	-11.51	0
-20	1.22	0	-14.01	0
-50	3.55	0	-16.75	0

5.3.6 Conclusions

The high contents of flavonoids and tannins in the bark material are claimed to be responsible for potential wound-healing effects due to antimicrobial, anti-inflammatory and cicatrizing effects. It was determined by calculating the DG, molecular orbital and electrostatic potential that the reaction mechanism is through attractions by hydrogen bonds between the OH group of the flavonoids and the C=O group of tannins.

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