INVESTIGATION OF INFLUENCE OF Z/E CONFIGURATION ON THE ANTI-OXIDANT AND ANTI-RADICAL ACTIVITIES OF LAPACHOL AND ITS DERIVATIVES: DFT ASSESSMENT

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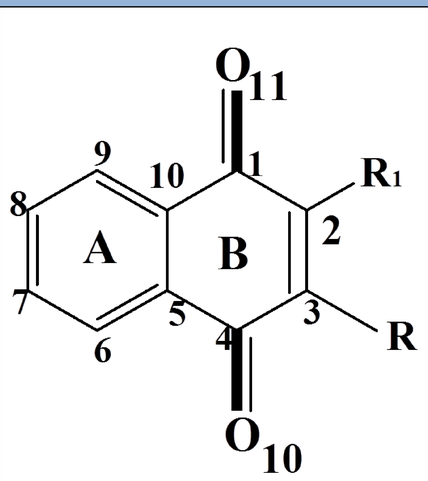
1-ABSTRACT

The geometry optimization of a series of twenty seven lapachol derivatives used for the treatment of carinosarcoma tumor (Walker 256) are performed at B3LYP/6-311++G(d,p) level in three distinct media (gas phase, water and acetonitrile). The migration from the E to the Z configuration or vice versa provokes a noticeable change in the O-H bond distance and potentially a remarkable alteration of the antioxidant activity. In addition, the majority of the E-configuration structures has shown a more pronounced antioxidant activity in solution (water and acetonitrile). In their various Z/E configurations, the 2-hydroxy-3-(2,3-dihydroxy-3-methylbutyl)-1,4-naphtoquinone compound bearing O…HO hydrogen bond (**La21 (HB)**) as well as the (2-hydroxy-3-(but-2-enyl)-1,4-naphtoquinone (**La6(HB)**) and 2-hydroxy-3-(3-methylpent-2-enyl)-1,4-naphtoquinone (**La7(HB)**) compounds have stronger antioxidant powers than classical bioactive compounds (caffeic acid, ferulic acid, p-coumaric acid, sinapic acid and vitamin C). On the whole, however, all Z-configuration compounds have a higher antiradical status compared to that of their E-configuration counterparts. From the global donor-acceptor mappings, the 2-hydroxy-3-(2,3-dihydroxy-3-methylbutyl)-1,4-naphtoquinone structure (**La21 (HB)**) has been elected as the best antiradical molecule of the series in the three study media. Its antiradical power has been detected to be higher than that of these five standard references adopted.

2-NEWTON RAPHTON GEOMETRY OPTIMIZATION

B3LYP/6-311++G(d,p))



Compounds	R_1	R
La_1	OH	$CH_2CH=C(CH3)_2$
La_2	OH	$CH=CHCH(CH_3)_2$
La_3	OH	$CH_2CH=C(Br)_2$
La_4	OH	$CH_2CH_2CH(CH_3)_2$
La_5	OH	$CH_2CH_2C(OH)(CH_3)_2$
La_6	OH	$CH=CHCH_2CH_3$
La_7	OH	$CH_2CH=C(CH_3)(C_2H_5)$
La_8	OH	$(CH_2)_2COOC_2H_5$
La_9	OH	$CH_2CH=C(C1)_2$
La_{10}	OAc	$CH_2CH=C(CH_3)_2$
La_{11}	OH	$CH_2CH=C(CH_2OH)CH_3$
La_{12}	CH_3	$CH_2CH=C(CH_3)_2$
La_{13}	OH	$CH_2CH=C(C_2H_5)_2$
La_{14}	H	$CH_2CH=C(CH_3)_2$
La_{15}	OH	$CH_2CH=C(C1)CH_3$
La_{16}	OCH_3	$CH_2CH=C(CH_3)_2$
La_{17}	OH	$CH=CBrC(CH_3)_2$
La_{18}	OH	$CH=C(CH_3)_2$
La_{19}	OH	$CH=CHCH_2CH_3$
La_{20}	OH	$CH_2CH=CH_2$
La_{21}	OH	$CH_2CH(OH)C(OH)(CH_3)_2$
La_{22}	NH_2	$CH_2CH=C(CH_3)_2$
La_{23}	OH	$CH_2CH=C(COOH)CH_3$
La_{24}	OH	$C(CH_3)_2CH=CH_2$
La_{25}	OH	$CH=CHCH_3$

3- RESULTS

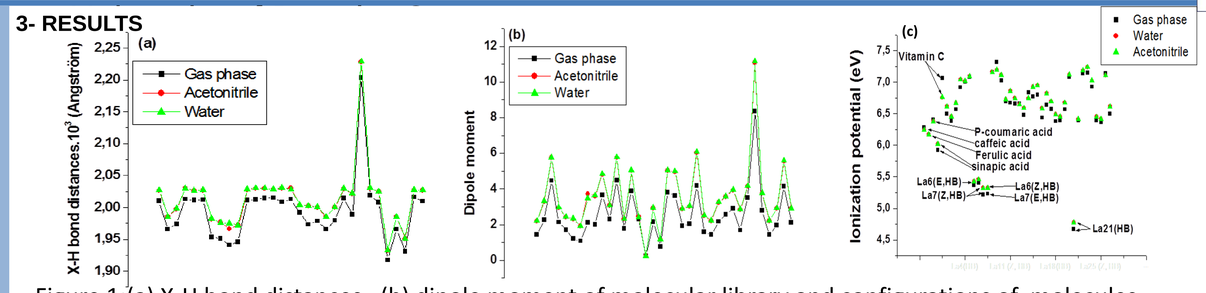


Figure 1:(a) X-H bond distances, (b) dipole moment of molecular library and configurations of molecules and those of classical bioactive compounds in various media(c)

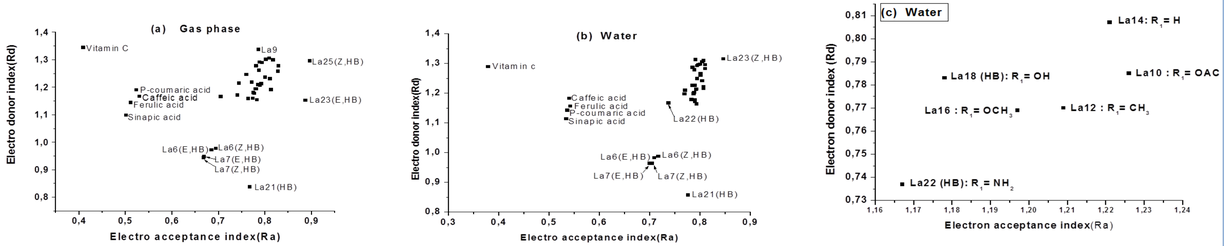


Fig.2:Complexation Global donor-acceptor mapping of the molecular library in various media integrating classical bioactive compounds

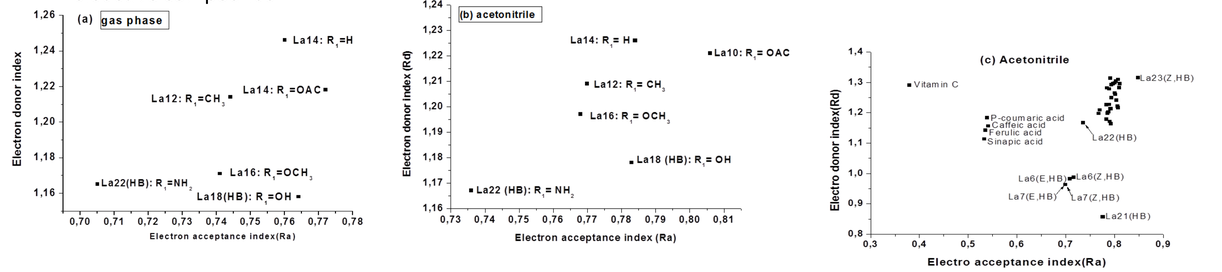


Fig.3:Donor-acceptor mapping based on modification of substituent (R_1) in various media.

4-Conclusion

In all the study media, the election of the 2-hydroxy-3-(2,3-dihydroxy-3-methylbutyl)-1,4-naphthoquinone structure as the most stable compound may result from the interaction between the hydrogen atom of the hydroxide group linked to the naphthalene ring and the double bond of the ethylenic linkage of the substituent R. Beyond the revealed evidence of possessing a more potent antioxidant power than the standard bioactive compounds (caffeic acid, ferulic acid, p-coumaric acid, sinapic acid and vitamin C), this **La21(HB)** compound was found to be a better electron donor than sodium. Overall, the influence of the E/Z configuration effect was found to be very noticeable in all three media.

5- References

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6-Aknowledgements

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