

## Topology analysis of six phytochemicals through ELF and LOL basins – A DFT study

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The topological features such as electron localization function (ELF) and local orbital locator (LOL) helps in analyzing the electron density based functions for identifying bonding interactions *via* local kinetic energies. The population magnitudes of basin attractor functions located around the atoms of the chosen compounds indicates the nature of the bonding interactions among the atoms with the aid of synaptic basins. The antioxidant activity of these natural biomolecules can be prevailed because of strong and weak covalent interactions. These interactions also play a vital role in the analysis of atomic shell structure, chemical bond classification and charge shift bond verifications.

**Keywords:** ELF basins, LOL, strong covalent, weak covalent interactions, BDE

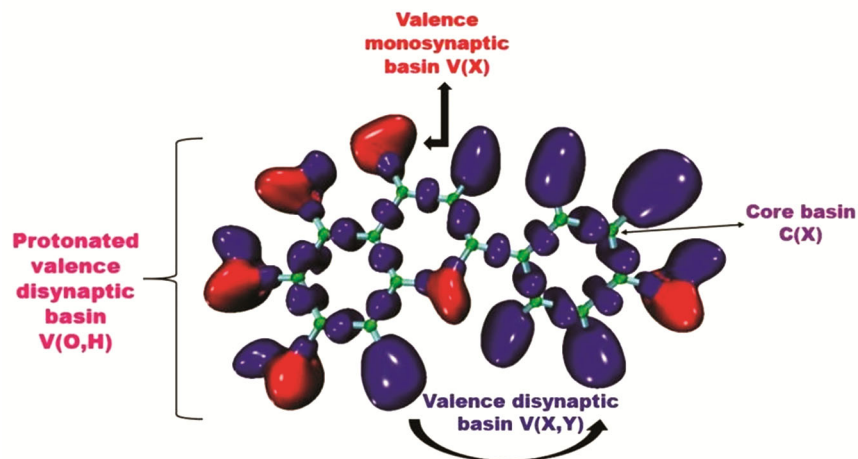
The radical scavenging nature of the biomolecules is mainly expressed in terms of easy charge transferring capacity. This charge donating ability of the compounds is nearly explained on the basis of the nature of the bond formed between them. If the strength of the bond is higher, the charge withdrawing ability is quiet lesser and *vice versa*. In order to find the characteristics of the bond formed, topological analyses are done. The outcomes of the topological analysis depict the nature and strength of the formed bond interaction *via* various parameters such as atoms in molecules (AIM) analysis, electron localization function (ELF), local orbital locator (LOL) *etc.* These topological analyses clearly explain the localization and delocalization of the charge density among them. Even though the other studies perceive attention, ELF and LOL play a major role through electron density in real space functions.

The quantum topological analysis named electron localization function (ELF) provokes the basic knowledge about the electron density. The ELF analysis helps in finding relative local kinetic energy *via* electron density. If the electron localization within the region is higher, the confinement of electrons in that region will be greater<sup>1</sup>. This exploration aids in exposing atomic shell structures, categorizes chemical bonds and in explaining charge shift bonds<sup>2,3</sup>. Higher magnitudes of ELF reveal the existence of covalent bonding, presence of solitary pair, whereas the lower

ELF magnitudes provide electron delocalization and in general, ELF measures the higher kinetic energy density by Pauli's repulsion.

The significance of ELF analysis is to show the basin attractors among the atoms which in turn yields the nature of the bonding in that system. The localization domains of the electrons are witnessed by the presence of local maxima (attractors) in ELF<sup>4,5</sup>. The three categories of domains of ELF basins are core basin, bonding and non-bonding valence basins. Within this frame work, the population of core basins acts as a K and L shell indicators. Further valence basins are effective tools to understand and interpret the characteristics of basic bonding between the atoms. The valence basins are labelled as V(X) monosynaptic basin which shares its boundaries with core basins and elucidates the presence of non-bonding interactions between the atoms. The next one shows the disynaptic basins V(X, Y), which segments its boundaries with the cores of two atoms X and Y<sup>6,7</sup> and the protonated disynaptic basins V(X, H), which portions its boundaries with the two atoms X and H as depicted in Scheme 1.

The synaptic order helps to find number of core basins that share their boundaries with the valence basins. The monosynaptic basins indicate the presence of lone pair of electrons in that zone and the disynaptic basins designates the bonding nature. The non-bonding and bonding interactions between the



Scheme 1 — Schematic representation of basins

atoms are exhibited by monosynaptic basin and disynaptic basin regions respectively<sup>8,9</sup>.

Localized orbital locator (LOL) is crucial factor for the explanation of the maximum gradient of localized orbitals observed during the overlapping of the orbitals. In addition to that, the LOL studies interpret the nature of chemical bonds between the atoms of the compound under investigation. Higher the LOL, the lower will be the agility of electrons and *vice versa*<sup>10</sup>. Both ELF and LOL investigations follows the kinetic energy density of electrons for the analyses of bonding and non-bonding interactions<sup>11,12</sup>. The existence of lone electron pairs in molecular zones is explicitly revealed by the attractor  $\Gamma$  regions between the connected atoms. These attractors are present in between the atoms and are interpreted in critical point attractors in LOL basins which show the higher local electron density<sup>13</sup>.

The most important aspect of analysing this topological investigation is to examine the atomic cores, predicting the presence of lone pairs, the nature and strength of the chemical bonding and the verification of charge shift of systems in the real space functions. Along with this, ELF tends to evidence in predicting the broad choice of bonding patterns. As it is a scalar function, its attractor functions of the corresponding basins are determined *via* gradient field topological analysis. Also, LOL studies enhance the pi-delocalization in perceptive manner. Furthermore, these two analyses also help in dealing with Pauli's repulsion *via* its high and low magnitudes. Consequently, the applicability of ELF to envisage the solitary pairs along with the interacting system instantly recommend the usage of ELF because

of its electronic structure properties rather than its dimensionality which are often called as quantum dots (QD)<sup>14</sup> (artificial atoms) which are relatively based on their charge density and its distribution.

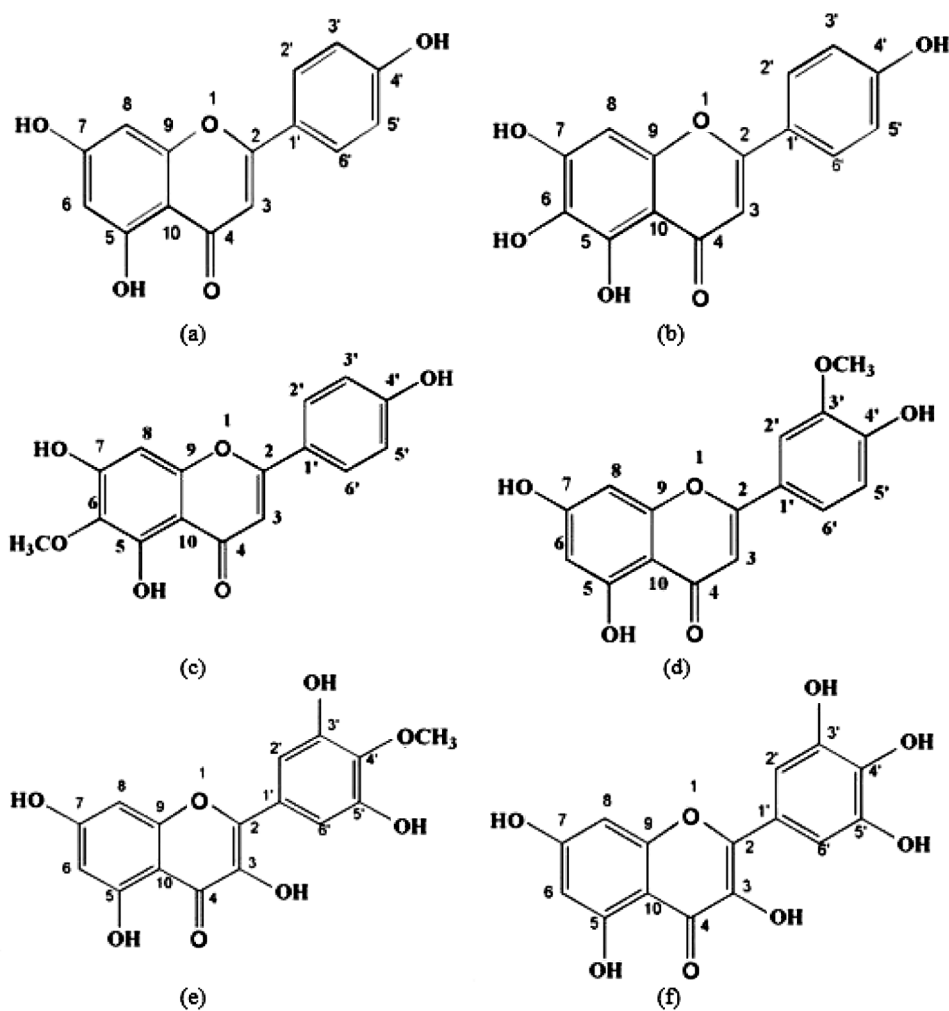
Both ELF and LOL clearly depict the strong and weak interaction zones for the compounds under study. The compounds which are undertaken for this investigation are of phytochemicals which are having potential antioxidant ability. ELF and LOL studies are used to predict the area of strong and weak covalent interaction within the compound of interest which helps to correlate the bond dissociation enthalpy (BDE) of a particular site with respect to the interactions obtained. All the chosen six compounds namely Apigenin (FA), Scutellarein (FS), Hispidulin (FH), Chrysoeriol (FC), Mearnsetin (FM) and Myrcetin (FMy) belong to flavone family and their structure along with atom numbering is depicted in Scheme 2.

### Computational Details

All theoretical computations such as geometry optimization and single point energy calculations for the neutral system is executed by Gaussian 16W suite *via* density functional theory (DFT) at M06-2X/6-311G(d,p) level of theory. The ELF and LOL basin attractors are examined using Multiwfn package<sup>15</sup> and are visualized by visual molecular dynamics (VMD) software.

### Results and Discussions

The ELF basin attractors among atoms present in molecules literally shows the characteristics of nature of bonding between them. The population range



Scheme 2 — Structure with atom number of (a) FA (b)FS (c) FH (d) FC (e) FM (f) FMY

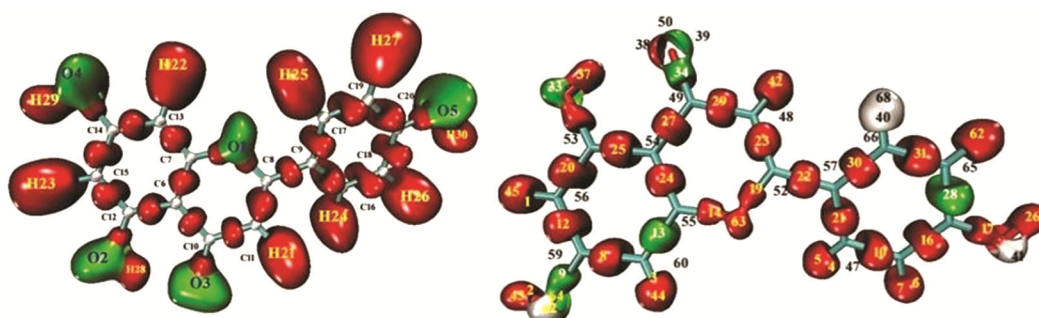


Fig. 1 — ELF and LOL basins of FA

obtained in the ELF basin attractors shows the type of basin functions.

In the case of FA (Fig. 1), the core basin attractors are observed near the carbon atoms. The single monosynaptic basin functions (green region) exist at  $O_1$  and  $O_2$  atoms labelled as  $V(O_1)$  and  $V(O_2)$ . A lone

pair of electron and corresponding non-bonding interaction at  $O_1$  and  $O_2$  atoms is due to the presence of single monosynaptic basin functions and the population range of such basin is 4.26e and 4.30e respectively. The presence of two monosynaptic in the same atom depicts the occurrence of two lone

pairs of electron within the atom and the same phenomenon is observed for O<sub>3</sub>, O<sub>4</sub> and O<sub>5</sub> atoms with the range of total electronic population as 5.41e, 4.42e and 4.43e respectively.

The electronic population of protonated disynaptic basins (green-red region) is observed at V(O<sub>2</sub>, H<sub>28</sub>), V(O<sub>4</sub>, H<sub>29</sub>) and V(O<sub>5</sub>, H<sub>30</sub>) with magnitudes of 1.82e, 1.76e and 1.744e, respectively. The disynaptic basin attractors between the C-O bonding also experiences lower population magnitudes and this demonstrates the delocalization of electron at O-H and C-O bonding. The other protonated disynaptic and disynaptic valence basins (red region) between the C-H and C-C atoms in the FA possess the electronic population greater than 2e and maximum electronic population is observed at V(C<sub>8</sub>, C<sub>11</sub>) as 3.47e. This series of electronic population designates the strong covalent nature of bonding between the atoms<sup>16</sup>.

Similarly, maximum LOL values are observed at the indices of 42, 43, 44, and 7 as 0.96, 0.95, 0.94, 0.95 Å, respectively. This is due to the contribution of electron in these sites for the formation of strong covalent bond. Conversely, least values are observed at the indices of 33, 38, 41, 67, 39, 14 as 0.59 and nearly around 0.60 Å, respectively which demonstrate weak covalent nature as shown in Fig. 1.

In FS (Fig. 2), the single monosynaptic basin function (red region) is observed only at O<sub>1</sub> represented as V(O<sub>1</sub>) with the population range of 4.27e clearly specifies the presence of a lone pair of electron and corresponding non-bonding nature. Further, two monosynaptic basins are observed for O<sub>2</sub>, O<sub>3</sub>, O<sub>4</sub>, O<sub>5</sub> and O<sub>6</sub> atoms with total electronic population as 4.4e, 4.52e, 4.43e, 5.41e and 4.45e, respectively depicts the occurrence of two lone pair of electrons.

The protonated disynaptic basins (red-blue region) is observed at V(O<sub>2</sub>, H<sub>28</sub>), V(O<sub>3</sub>, H<sub>29</sub>), V(O<sub>4</sub>, H<sub>30</sub>) and V(O<sub>6</sub>, H<sub>31</sub>) with electronic population of 1.79e, 1.73e,

1.75e and 1.74e, respectively displays the bonding between one monosynaptic basin of highly electronegative atom with H atom leading to weak covalent interaction. Further, the population range of other valence disynaptic basins between C-O is also lower in values. Additionally, some other protonated disynaptic (C-H) atoms and disynaptic valence basins (C-C) in the compounds (blue region) possess the electronic population values greater than 2e and V(C<sub>9</sub>, C<sub>13</sub>) indicates the stronger nature of covalent interaction.

Likewise, 7, 53, 45, 43, 38, 37, 5, 6 and 3 indices register the magnitude for LOL as 0.97, 0.98, and 0.92 Å, respectively as shown in Fig. 2 which in turn establishes the covalent bond interactions. Likewise, the indices 35, 52, 72, 71, 2, 11, 14, 15, 40, 42, 46, 48 have weaker interactions with magnitudes of 0.59 (first two indices) and 0.60 Å (remaining), respectively.

The low magnitudes of the ELF and LOL magnitudes at the foresaid sites possess weak covalent interactions which can transfer its charges more easily than that of strong covalent regions. Likewise, those specific sites also attain lower BDE magnitudes that are more prone for the H atom abstraction. That way, it shows that the BDE magnitudes and the simulated ELF analysis are in good agreement with each other for FA and FS<sup>17</sup>.

In FH, the non-bonding single monosynaptic basin function (green zone) is observed at three atomic sites O<sub>1</sub>, O<sub>3</sub> and O<sub>6</sub> as depicted in Fig. 3 and are branded as V(O<sub>1</sub>), V(O<sub>3</sub>) and V(O<sub>6</sub>) with the population range of 4.25e, 4.35e and 4.47e respectively, which clearly indicates the presence of a lone pair of electron in such atoms. Two monosynaptic basins are observed at O<sub>2</sub>, O<sub>4</sub> and O<sub>5</sub> atoms with the range of total electronic population as 4.8e, 4.41e and 5.42e, respectively, indicates the two lone pair of electrons around them. The electronic

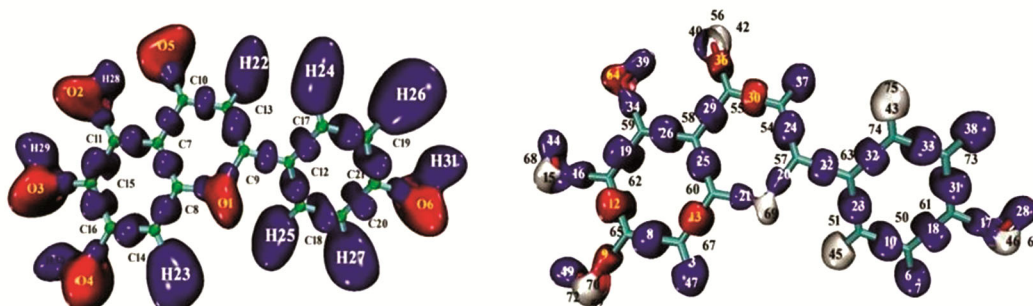


Fig. 2 — ELF and LOL basins of FS

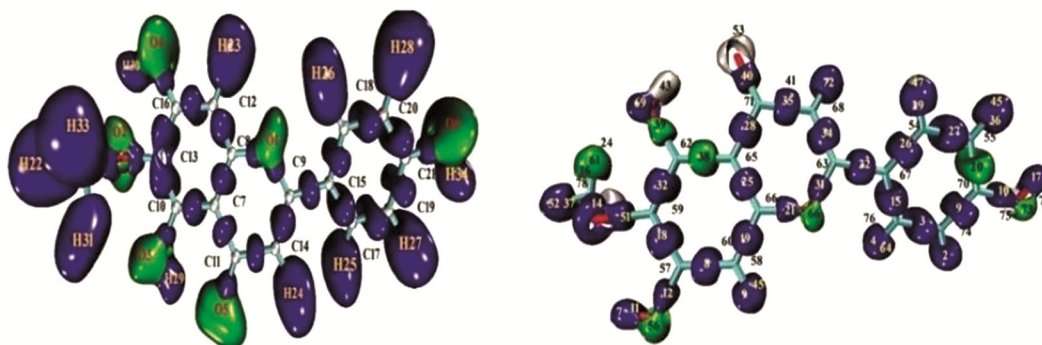


Fig. 3 — ELF and LOL basins of FH

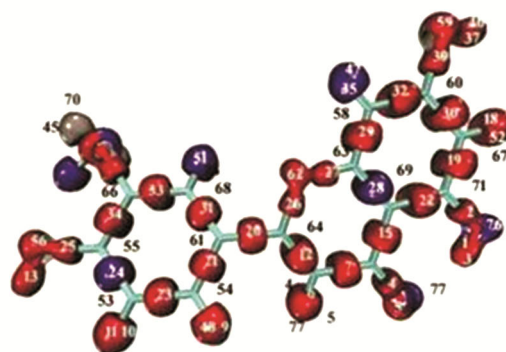


Fig. 4 — ELF and LOL basins of FC

population of protonated disynaptic basins (blue-green zone) are observed at  $V(O_3, H_{29})$ ,  $V(O_4, H_{30})$  and  $V(O_6, H_{34})$  shows about 1.81e, 1.76e and 1.74e, respectively. Of course, the above said characteristics are also found to exist at C-O site. Further the electron delocalization occurs at both the sites of O-H and C-O. Similarly, the larger population magnitudes are perceived at the other protonated disynaptic (C-H) and some other disynaptic basin (blue zone) functions (C-C) nearly exceeds 2e. The valence disynaptic basin  $V(C_9, C_{14})$  acquires maximum magnitude (3.465e) and shows the highest covalent interactions.

Correspondingly, LOL investigation provides the maximum LOL magnitudes at the indices of 2 (0.93 Å), 11 (0.95 Å), 37 (0.93 Å), 42 (0.92 Å), 47 (0.92 Å) and 64 (0.94 Å) which designates the covalent bonding interactions between the shared electrons. The least LOL values are observed at the indices 39 (0.59 Å), 50 (0.59 Å) and 75 (0.59 Å). In addition to that, 0.62 Å is observed at the indices 1, 6, 13, 24, 44, 46 and 77 as depicted in Fig. 3. All other indices are falling within the range of 0.7 Å to 0.8 Å.

In FC, the non-bonded single lone pair of electron (blue zone) is found at  $O_1$  and  $O_2$  with the valence

monosynaptic population values categorized as  $V(O_1)$  being 4.26e and  $V(O_2)$  being 4.33e. The two lone pairs of electrons found near the other oxygen atoms in the compound namely at  $V(O_3)$ ,  $V(O_4)$ ,  $V(O_5)$  and  $V(O_6)$  yielded with total electronic population values of 4.8e, 5.41e, 4.43 and 4.46e, respectively. Some protonated disynaptic (blue-red zone) basins (Fig. 4) such as  $V(O_2, H_{29})$ ,  $V(O_5, H_{30})$  and  $V(O_6, H_{31})$  possess low electronic population values as 1.82e, 1.76e, 1.74e, respectively. In addition to that other delocalization sites (C-O bond interactions) have electronic population more than 1e. The C-H (other protonated disynaptic) and C-C (disynaptic basin) own maximum electronic population (red zone) representing the strong covalent interactions between them.

In the same way, LOL analysis exhibits maximum values at the indices 48, 80, 79, 75, 57, 3, 8, 9, 10, 11, 18, 36, 43 and 47 indicated in Fig. 4 as 0.96, 0.95, 0.93, 0.92 Å respectively which in turn reveal the strong covalent bond interactions. Further the indices 2, 50, 49, 65, 4, 25, 27, 38, 42 and 49 possess lower LOL magnitudes.

Similarly, in this case also, the least ELF and LOL magnitudes are reported at the sites which also

attain minimum dissociation energy leading to the zone for ease charge donating ability than that of other zones. From this, it is proved that the published BDE magnitudes are in good agreement with the replicated ELF analysis for FH and FC<sup>18</sup>.

In the case of FM, ELF basin attractors (Fig. 5), O<sub>1</sub>, O<sub>3</sub> and O<sub>8</sub> are represented as V(O<sub>1</sub>), V(O<sub>3</sub>) and V(O<sub>8</sub>) within the population range of 4.33e, 4.32e and 4.43e respectively, indicating the presence of single lone pair of electron which corresponds to non-bonding (blue zone) nature in those sites. Two monosynaptic basins are observed for O<sub>2</sub>, O<sub>4</sub>, O<sub>5</sub>, O<sub>6</sub> and O<sub>7</sub> atoms with total electronic population as 4.47e, 4.83e, 5.39e, 4.45e and 4.47e, respectively illustrating the occurrence of two monosynaptic basins in the same atom and specifies the existence of two lone pair of electrons. The V(O<sub>2</sub>, H<sub>29</sub>), V(O<sub>3</sub>, H<sub>30</sub>), V(O<sub>6</sub>, H<sub>31</sub>), V(O<sub>7</sub>, H<sub>32</sub>) and V(O<sub>8</sub>, H<sub>33</sub>) labelled protonated disynaptic basins (green-blue zone) exhibits least population magnitudes at 1.74e, 1.83e, 1.75e, 1.74e and 1.76e respectively. The same trend is observed for C-O interactions also and parades lower magnitude and depicts weaker covalent interactions. The C-H and C-C bonding sites (green zone) reveal maximum population values and indicates sturdier covalent interactions.

In the same manner, the indices 48, 36, 4, 5, 31, 40, 45, 57, 83 and 85 shown in the Fig. 5 have minimum

LOL magnitudes of the order of 0.59 (first two indices) and 0.60 Å (remaining indices) and the corresponding indices are 37 (0.97 Å), 49 (0.96 Å) and 2 (0.95 Å) and are observed to have maximum LOL values. The maximum and minimum LOL magnitudes denote the strong and weaker covalent interactions respectively.

The secondary metabolite FM<sub>y</sub> shows the single monosynaptic basin function (red zone) at the O<sub>1</sub> and O<sub>3</sub> atoms written off as V(O<sub>1</sub>) and V(O<sub>3</sub>) with the population range of 4.32e and 4.32e, respectively confirming the existence of a lone pair of non-bonding electron in that atoms. The oxygen atoms O<sub>2</sub>(4.48e), O<sub>4</sub>(5.38), O<sub>5</sub>(4.43), O<sub>6</sub>(4.44e), O<sub>7</sub>(4.44e) and O<sub>8</sub>(4.62e) characterize the existence of two lone electron pairs in that atom. The protonated disynaptic basins (red-green zone) observed at the oxygen and hydrogen atoms shows the lower magnitude at V(O<sub>8</sub>, H<sub>33</sub>) as 1.69e which indicates the presence of weaker covalent interactions between them. The other protonated O-H basin such as V(O<sub>2</sub>, H<sub>28</sub>), V(O<sub>3</sub>, H<sub>29</sub>), V(O<sub>5</sub>, H<sub>30</sub>), V(O<sub>6</sub>, H<sub>31</sub>) and V(O<sub>7</sub>, H<sub>32</sub>) along with the C-O bond interactions also exhibit lower values (greater than 1e) than the other C-H and C-C interactions (green zone) which are greater than 2e categorizing stronger interactions.

Correspondingly, the lower levels of LOL are observed at the indices (Fig. 6) 1, 53, 69, 83, 80, 56,

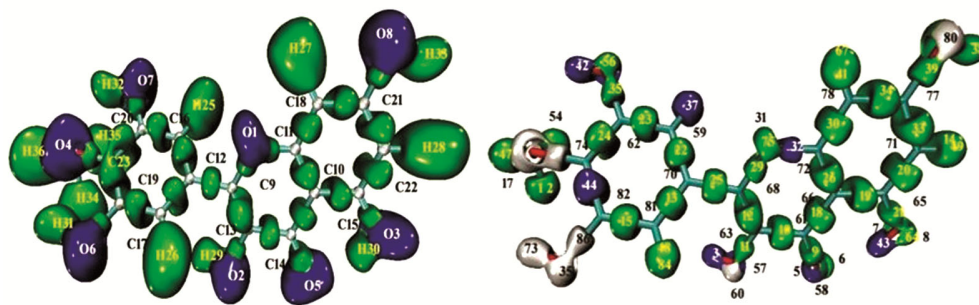


Fig. 5 — ELF and LOL basins of FM

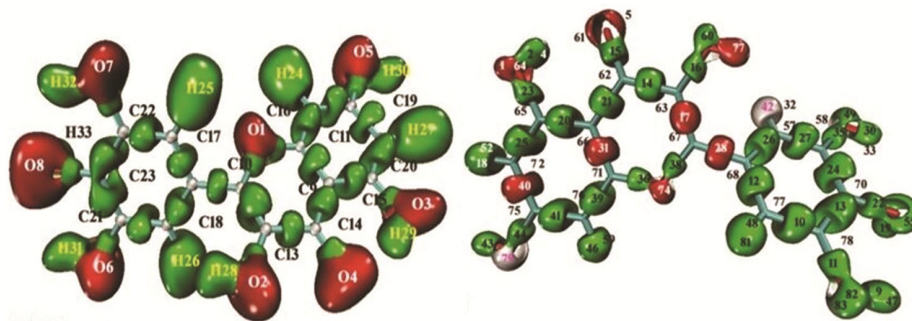


Fig. 6 — ELF and LOL basins of FM<sub>y</sub>

51, 49, 45, 37, 34, 29, 19, 8, 6, 3 as 0.59Å and 0.60Å, respectively, and confirm the presence of weaker covalent interactions at those indices. The maximum LOL values are given at the indices 33 (0.95A°), 42(0.93A°), 81 (0.94A°) and 59 (0.94A°) reveals the existence of strong covalent bonding.

Here in the case of FM and FM<sub>y</sub>, the minimum ELF and LOL ranges are observed at the above said basins and it clearly reveals the presence of weaker interaction between the atoms which are alike with the least BDE quantities. Like the previous four compounds, this compound also satisfies the least ELF and LOL magnitude with least BDE magnitudes exposed in the published results<sup>19</sup>.

### Conclusion

The strong and weak covalent interactions are elucidated through topological studies for six phytochemicals by way of ELF and LOL basin analysis. The basin attractor functions obtained from the ELF and the indices attained through LOL helps in understanding the interactions between the atoms of these compounds. The basin attractors obtained from these six compounds distinguishes between the strong and weak covalent interactions. The results obtained from the ELF analysis are in accordance with the published BDE magnitudes.

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