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# Molecular Docking and Molecular Dynamics Simulation Studies of Triterpenes from *Vernonia patula* with the Cannabinoid Type 1 Receptor

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**Abstract:** A molecular docking approach was employed to evaluate the binding affinity of six triterpenes, namely epifriedelanol, friedelin, α-amyrin, α-amyrin acetate, β-amyrin acetate and bauerenyl acetate, towards the cannabinoid type 1 receptor (CB1). Molecular docking studies showed that friedelin, α-amyrin and epifriedelanol had the strongest binding affinity towards CB1. Molecular dynamics simulation studies revealed that friedelin and α-amyrin engaged in stable non-bonding interactions by binding to a pocket close to the active site on the surface of the CB1 target protein. The studied triterpenes showed a good capacity to penetrate the blood-brain barrier. These results help to provide some evidence to justify, at least in part, the previously reported antinociceptive and sedative properties of *Vernonia patula*.

**Keywords:** molecular docking; molecular dynamics; triterpenes; *Vernonia patula*

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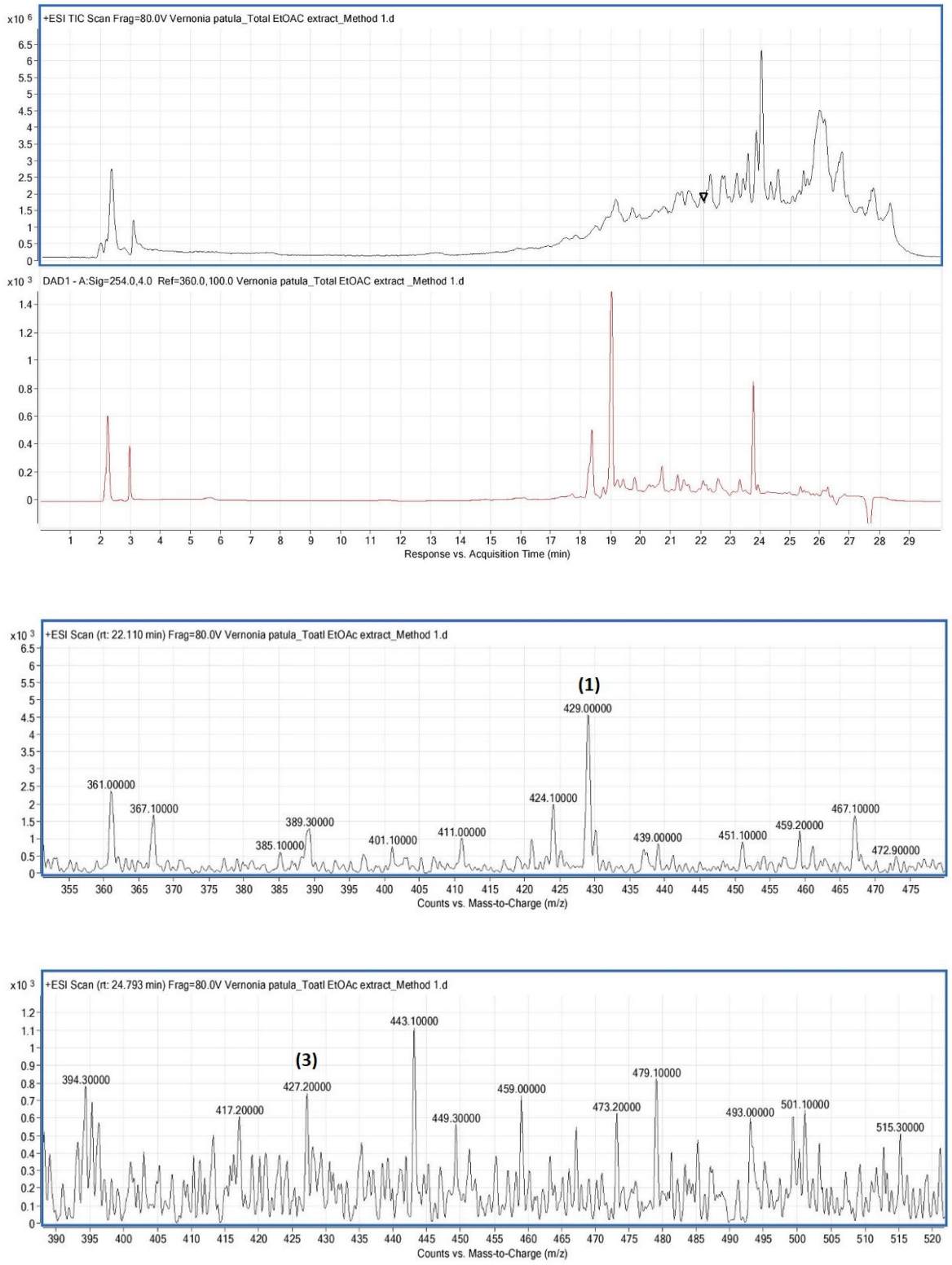


**Figure 1.** Detection of epifriedelanol (**1**) and $\alpha$-amyrin (**3**) in VP (fraction 1) using HPLC-DAD-MS analysis.

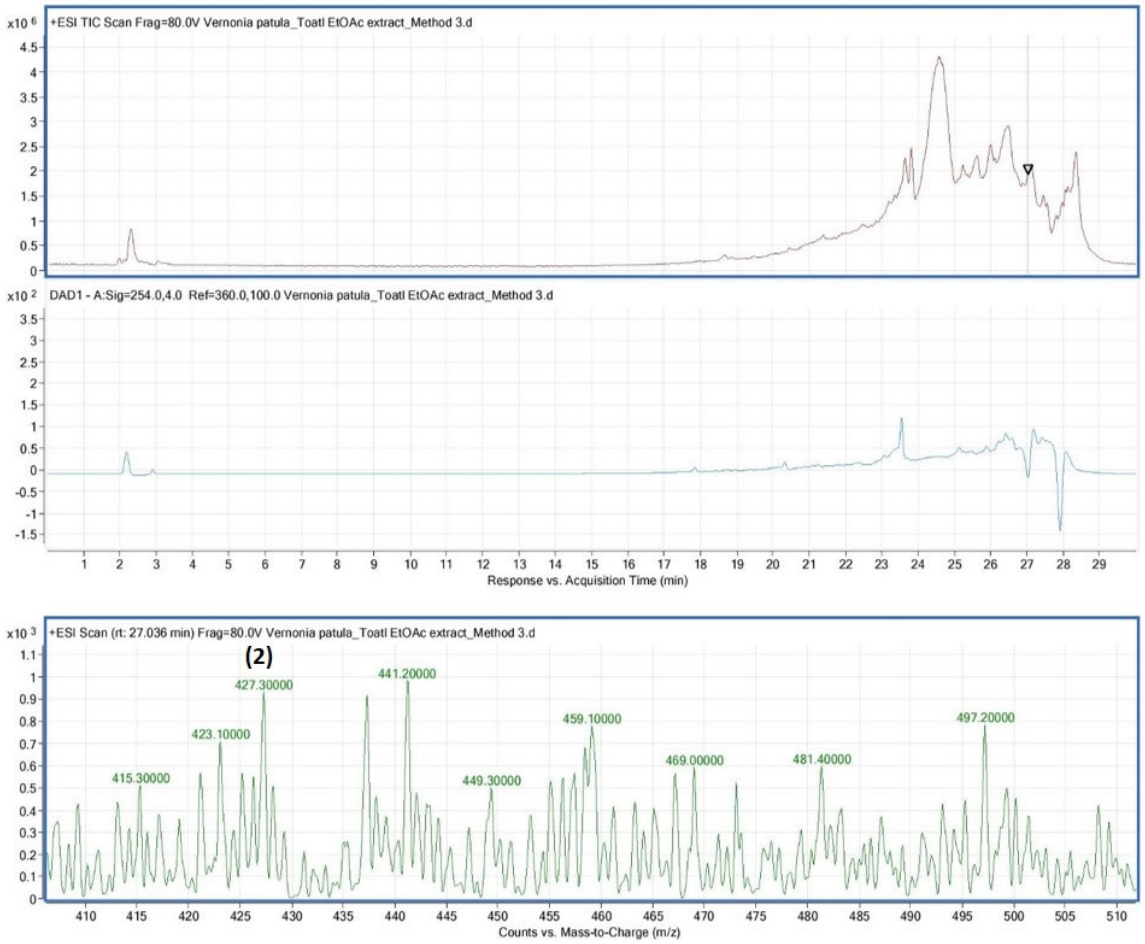


**Figure 2.** Detection of friedelin (**2**) in VP (fraction 3) using HPLC-DAD-MS analysis.

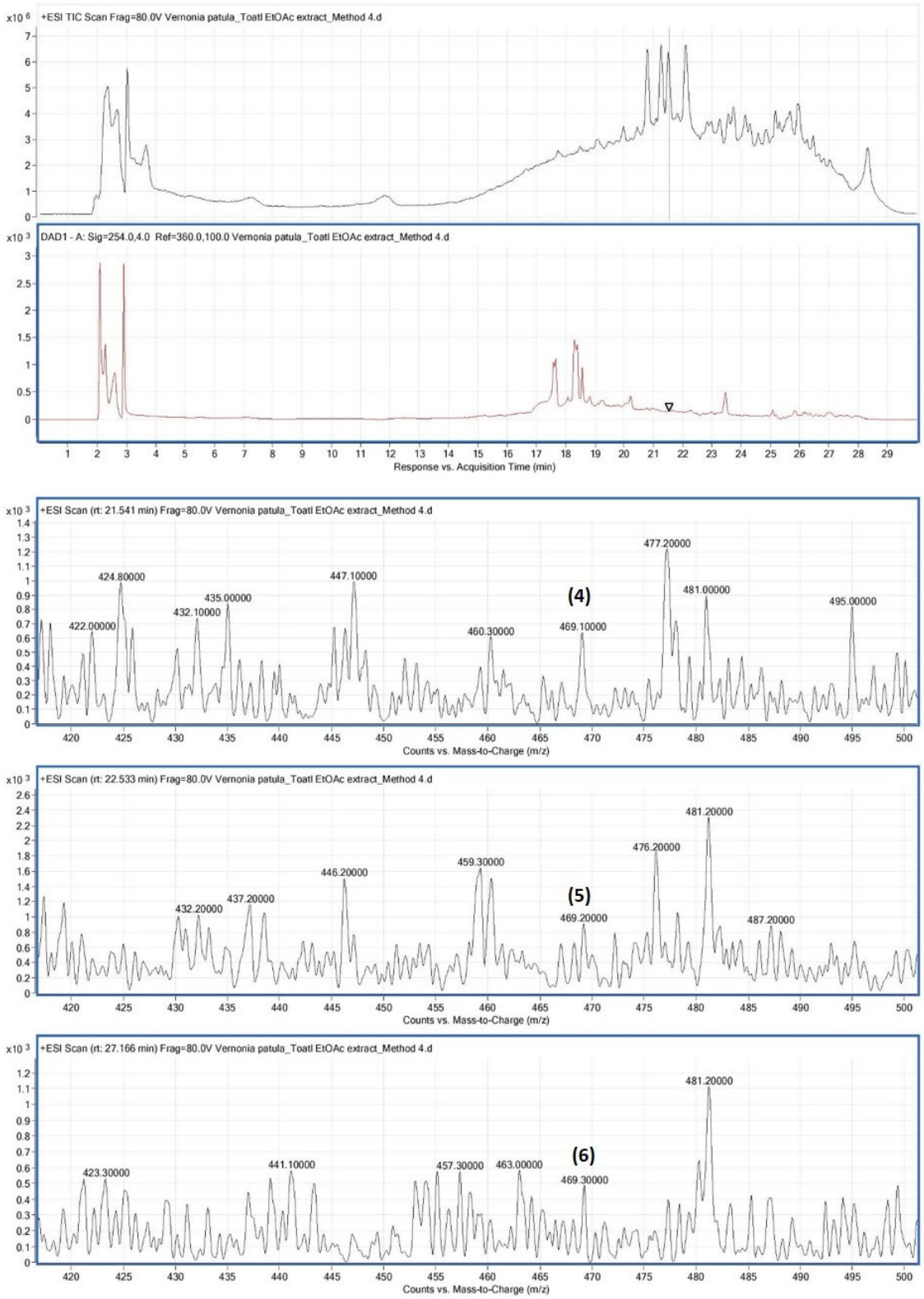


**Figure 3.** Detection of $\alpha$-amyrin acetate (**4**), β-amyrin acetate (**5**) and bauerenyl acetate (**6**) in VP (fraction 4) using HPLC-DAD-MS analysis.

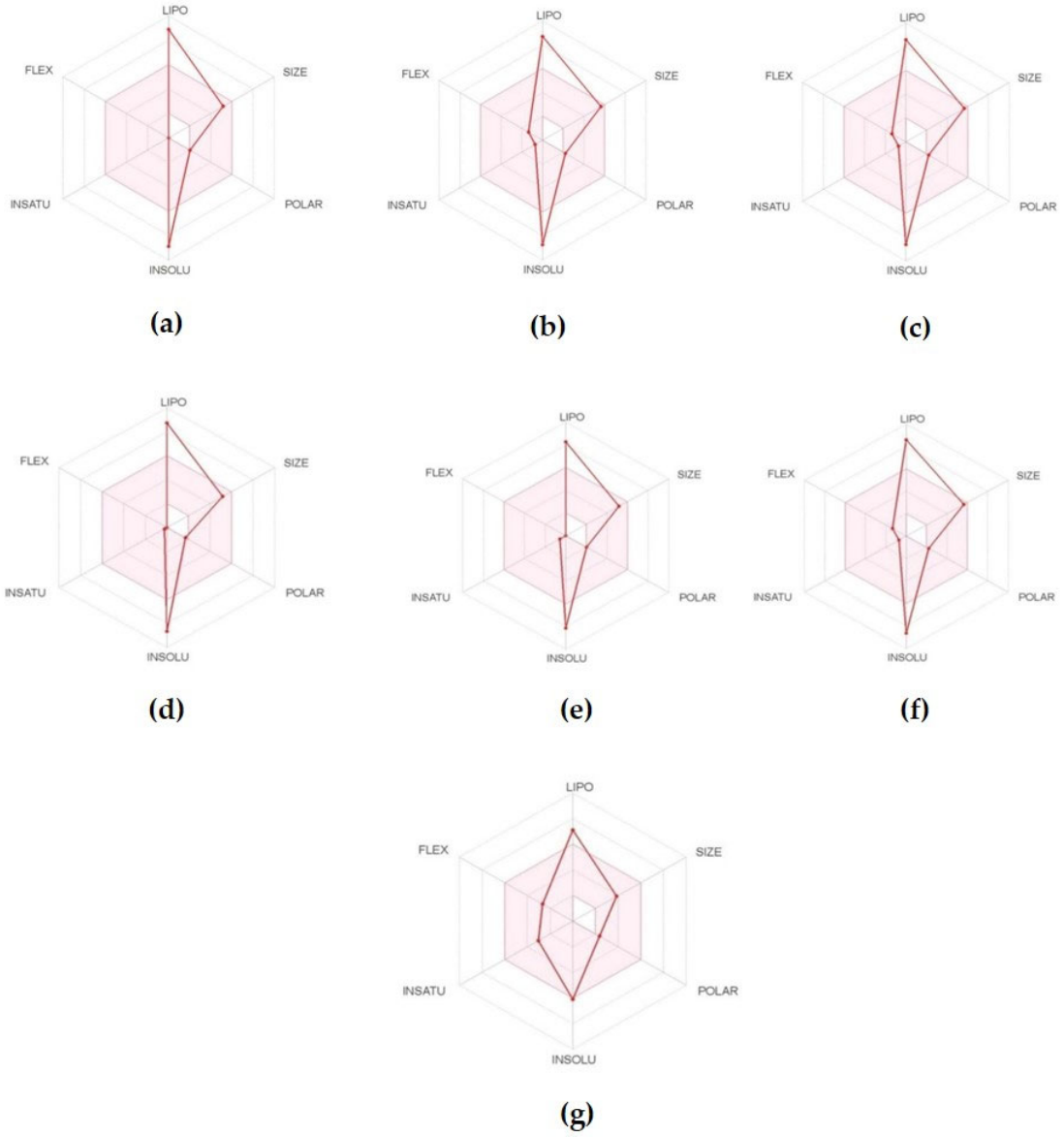


**Figure 4.** Bioavailability Radar plots of (**a**) epifriedelanol; (**b**) β amyrin acetate; (**c**) bauerenyl acetate; (**d**) friedelin; (**e**) α-amyrin; (**f**) α- amyrin acetate; (**g**) THC. LIPO- lipophilicity, INSOLU- insolubility, and FLEX- flexibility.

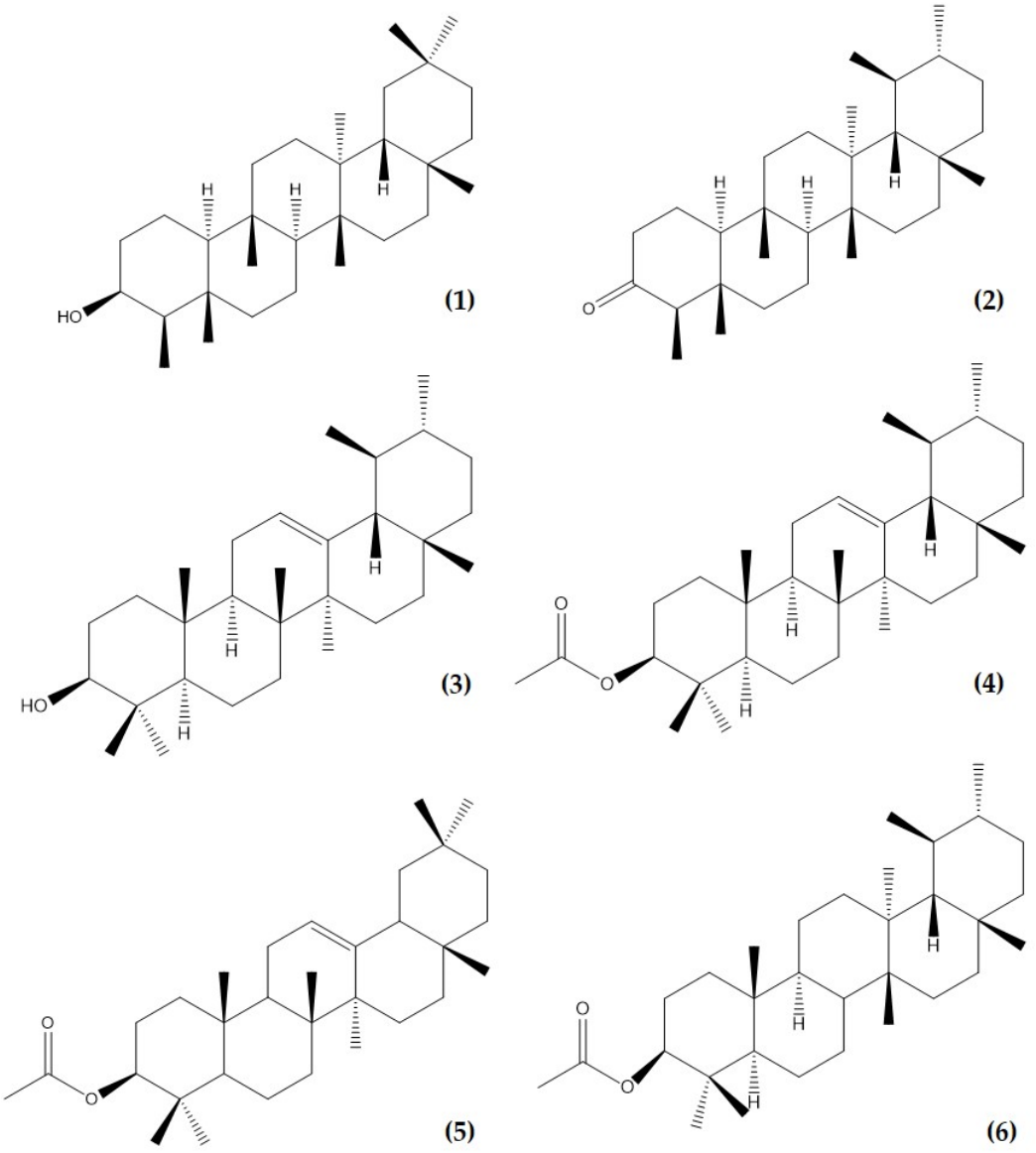


**Figure 5.** Structures of VP triterpenes. Epifriedelanol (**1**), friedelin (**2**), α- amyrin (**3**), α-amyrin acetate (**4**), β-amyrin acetate (**5**) and bauerenyl acetate (**6**).

**Table 1.** Intermolecular interactions of α-amyrin acetate, β-amyrin acetate and bauerenyl acetate with CB1.

| Ligand | Binding affinity (kcal/mol) | Binding residues | Category | Type | Distance (Å) |
|---|---|---|---|---|---|
| α-amyrin acetate | –7.8 | Ala118 | Hydrophobic | Alkyl | 3.68 |
| | | Ala118 | Hydrophobic | Alkyl | 3.42 |
| | | Ile119 | Hydrophobic | Alkyl | 4.38 |
| | | Leu122 | Hydrophobic | Alkyl | 4.38 |
| | | Leu122 | Hydrophobic | Alkyl | 5.23 |
| | | Leu126 | Hydrophobic | Alkyl | 4.63 |
| | | Ile119 | Hydrophobic | Alkyl | 4.89 |
| | | Leu122 | Hydrophobic | Alkyl | 4.63 |
| | | Met384 | Hydrophobic | Alkyl | 4.22 |
| | | Leu126 | Hydrophobic | Alkyl | 5.49 |
| | | Met384 | Hydrophobic | Alkyl | 3.92 |
| | | Ile119 | Hydrophobic | Alkyl | 4.65 |
| | | Leu388 | Hydrophobic | Alkyl | 3.67 |
| | | Leu122 | Hydrophobic | Alkyl | 5.12 |
| | | Ile119 | Hydrophobic | Alkyl | 4.53 |
| | | Phe381 | Hydrophobic | Pi-Alkyl | 4.10 |
| | | Phe381 | Hydrophobic | Pi-Alkyl | 3.94 |
| β-amyrin acetate | –7.3 | Gln115 | Hydrogen Bond | Conventional | 3.06 |
| | | Leu122 | Hydrophobic | Alkyl | 5.23 |
| | | Met384 | Hydrophobic | Alkyl | 4.81 |
| | | Leu385 | Hydrophobic | Alkyl | 4.41 |
| | | Leu388 | Hydrophobic | Alkyl | 4.59 |
| | | Leu126 | Hydrophobic | Alkyl | 5.06 |
| | | Met384 | Hydrophobic | Alkyl | 4.37 |
| | | Leu122 | Hydrophobic | Alkyl | 5.00 |
| | | Ile119 | Hydrophobic | Alkyl | 4.93 |
| | | Leu122 | Hydrophobic | Alkyl | 4.12 |
| | | Phe381 | Hydrophobic | Pi-Alkyl | 5.26 |
| | | Phe381 | Hydrophobic | Pi-Alkyl | 4.96 |
| | | Phe381 | Hydrophobic | Pi-Alkyl | 5.23 |
| | | Phe381 | Hydrophobic | Pi-Alkyl | 4.53 |
| Bau-erenyl acetate | –7.5 | Ala120 | Hydrophobic | Alkyl | 3.58 |
| | | Val179 | Hydrophobic | Alkyl | 4.99 |
| | | Ala120 | Hydrophobic | Alkyl | 4.75 |
| | | Ala120 | Hydrophobic | Alkyl | 4.18 |
| | | Val179 | Hydrophobic | Alkyl | 5.37 |
| | | Phe177 | Hydrophobic | Pi-Alkyl | 4.57 |
| | | His178 | Hydrophobic | Pi-Alkyl | 4.56 |
| | | His178 | Hydrophobic | Pi-Alkyl | 4.60 |
| | | His178 | Hydrophobic | Pi-Alkyl | 4.95 |
| | | His178 | Hydrophobic | Pi-Alkyl | 4.52 |