

Molecular Docking Analysis of Compounds *Lavandula angustifolia* Mill with Gaba_A Receptor Lessen Stress

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GABAA receptors are hetero-oligomeric Cl channels that are elective blocked by the alkaloid bicuculline and modulated by steroids, barbiturates and benzodiazepines. The anticonvulsant activity of diazepam and phenobarbital may be mediated in Section by enhancement of inhibition involving γ -aminobutyric acid (GABA). Lavender is one of the maximum effective medicinal plants various therapeutic effects of lavender, so as sedative, spasmolytic, antiviral, and antibacterial activities have been reportage. The molecular docking analysis done indicates that the receptor of GABA interaction with the *Lavandula angustifolia* Mill compounds effectively. Ligand *Lavandula angustifolia* Mill compounds with GABAA are safer and milder with fewer or no side effects than the drugs currently used in the remedy of lessening high Stress which can be better for the development of new therapeutics to blocked GABAA lessening stress. Results conûrm all the *Lavandula angustifolia* Mill compounds were good binding energy when compared with the binging energies of diazepam (-295.80) Among all the *Lavandula angustifolia* Mill compounds, the indicate nigh binding energy value (-256.12).

Key word: Hex (6.1), *Lavandula angustifolia* Mill, Docking, GABAA receptors.

True lavender (*Lavandula angustifolia* Mill. syn. *L. officinalis* Chaix) is a perennial shrub of the family Lamiaceae. It is native to southern Europe and the Mediterranean area and is commercially cultivated in France, Spain, Portugal Hungary, the UK, Bulgaria, Australia, China and the USA¹. This plant is cultivated primarily for its aromatic inflorescence from which the essential oil is isolated, although its fresh and dried flowers

are also marketed². Lavender oil is known for its excellent aroma and is extensively used in the perfumery, flavour and cosmetic industries. The oil is known to possess sedative, carminative, anti-depressive and anti-inflammatory properties. It was also found to be active against many species of bacteria, including those resistant to antibiotics, such as methicillin-resistant *Staphylococcus aureus* and vancomycin-resistant *Enterococcus*³. Lavender oil is known for to be an effective antifungal agent against *Aspergillus nidulans* and *Trichophyton Mentagrophytes*⁴. Lavender's essential oil is commonly used in aromatherapy and massage. Its major clinical benefits are on the central nervous system. Many studies conducted on both animals and

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humans support its use as a sedative, anxiolytic and mood modulator. Particular chemical constituents of lavender have potent anticarcinogenic and analgesic properties. Aromatherapy with lavender oil has been recommended to treat a wide range of ailments including stress, anxiety depression, fatigue, motion sickness, and hypertension⁵. In the mammalian focal nervous system, GABA is the main inhibitory neurotransmitter. Conformationally restricted analogues of GABA have been used to assist in identifying three basic GABA receptors, called GABAA, GABAB and GABCB receptors. Lavender's essential oil is that which exerts anxiolytic, sedative, anticonvulsant and most of these effects are thought to result from a facilitation of the action of gamma aminobutyric acid (GABA), an inhibitory neurotransmitter in the central nervous system. γ -Aminobutyrate (GABA) is a major inhibitory neurotransmitter in the adult mammalian brain. GABA is also considered to be a multifunctional molecule that has different situational functions in the central nervous system, the peripheral nervous system, and in some nonneuronal tissues. GABA is formed within GABAergic axon terminals and released into the synapse, where it acts at one of two types of receptor GABAA which controls chloride entry into the cell, and GABAB, which increases potassium conductance, decreases calcium entry, and inhibits the presynaptic release of other neurotransmitters⁶. In the brain, 17-20% of all neurons are GABAergic and most of the physiological activities of GABA are generated through GABAA receptors (GABAA-Rs). These ionotropic receptors or ligand-gated ion channel (LGIC) are chloride anion (Cl⁻) channels that can be opened and activated by the endogenous neurotransmitter GABA and several drug classes, including benzodiazepines, barbiturates, steroids, anesthetics and convulsants. As the primary receptor for GABA in the CNS, GABA_A receptors are involved in a variety of behavioral and cognitive processes⁷. Diazepam is a benzodiazepine that binds to a specific subunit on the GABA receptor at a site that is distinct from the binding site of the endogenous GABA molecule. The GABA receptor is an inhibitory channel which, when activated, decreases neuronal activity. Because of the role of diazepam as a positive allosteric modulator of GABA, when it binds to benzodiazepine receptors it causes inhibitory effects. This arises from the

hyperpolarization of the post-synaptic membrane owing to the control exerted over negative chloride ions by GABAA receptors. The purpose of this experiment was to evaluate the activity and reduce nerve pain sedation lavender plants and its effects on the central nervous system of the GABA_A receptor.

MATERIAL AND METHODS

Molecular docking

Bioinformatics is seen as an emerging field with the potential to significantly improve how drugs are found and brought to the clinical trials and eventually released to the marketplace. The docking analysis was carried by HEX docking software. Hex is calculated protein-ligand docking, and it can superpose pairs of molecules using only fitting of their 3D shapes. It avails Spherical Polar Fourier (SPF) correlations to accelerate the calculations and is one of the few docking programs which has built in graphics to view the effect^{8,9}. Docking permits the scientist to virtually screen a database of compounds and bode the strongest binders based on variant scoring functions.

It explores ways in which two molecules, such as *Lavandula angustifolia* Mill compounds and GABAA receptor (Fig. 1) fit together and dock to each other well. The collection of *Lavandula angustifolia* Mill compounds and GABAA receptor was discovered via docking and their relative stabilities were evaluated using molecular dynamics and their binding affinities, using free energy simulations. The parameters applied for the docking process via HEX docking were:

- Correlation type – Shape only
- FFT Mode – 3D fast life
- Grid Dimension – 0.6
- Receptor range – 180
- Ligand Range – 180
- Twist range – 360
- Distance Range – 40

Also the parameters applied for the matching process via HEX matching were:

RESULTS AND DISCUSSION

Molecular docking results of the *Lavandula angustifolia* Mill compounds ligand (Linalool, linalyl acetate, lavandulyl acetate, α -terpineol and

geranyl acetate) with the GABA_A nerve receptors obtained using Hex are shown in Table 1.

Prediction of interaction energies between ligand and receptor has been a major challenge for molecular docking. Hex uses scoring algorithms to calculate these energy values of the docked complexes and stability of the docked complexes increases with decrease in energy value. While comparing the results obtained with all the

Lavandula angustifolia Mill compounds ligand it is prominent that all of them show better stability when docked with GABA_A nerve receptor. It is noted that the energy value is comparatively less for the modeled structure of geranyl acetate than other *Lavandula angustifolia* Mill compounds with the energy matching value of (-256.12) hence conforming highest stability (Fig 2).

Table 1. Results of molecular docking of the the *Lavandula angustifolia* Mill compounds with GABA_A nerve receptors using the hex along with intermolecular bonding information

Receptor	Ligand	R _{Docking}	E _{Docking}	R _{Maching}	E _{Maching}
GABA _A nerve receptors	Diazpeam	11.6	-295.80	6.4	-391.56
	Linalool	10.4	-209.85	7.2	-359.42
	linalylacetate	10.4	-248.29	8.2	-361.88
	lavandulyl acetate	10.8	-228.21	7.2	-372.72
	α-terpineol	11.2	-188.16	6.4	-347.48
	geranyl acetate	9.6	-256.12	6.4	-397.31

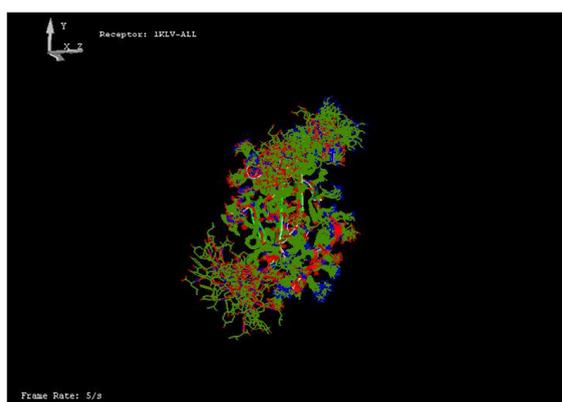


Fig. 1. GABA_A receptor

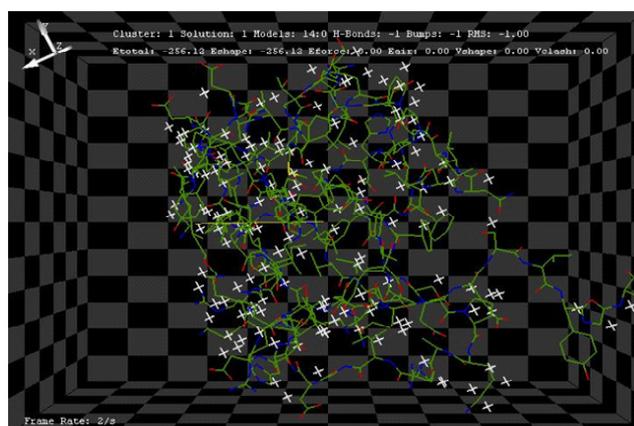


Fig. 2. Interaction and binding energy of geranyl acetate with GABA_A nerve receptor

CONCLUSION

The receptor-ligand interactions play a significant role in molecular docking and drug designing. The receptor of GABAA interacts with the Linalool, linalyl acetate, lavandulyl acetate, α -terpineol and geranyl acetate effectively. The *Lavandula angustifolia* Mill compounds ligand (Linalool, linalyl acetate, lavandulyl acetate, α -terpineol and geranyl acetate) are safer and milder with fewer or no side effects than the drugs currently used in the treatment of lessening high lessen Stress. Therefore *angustifolia* Mill compounds ligand can be better used for the development of new therapeutics to decrease formation of GABAA.

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