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Theoretical evaluation of some natural polysaccharides as nanocarriers for the terpene alcohols from essential oils

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Abstract. Essential oils have attracted a continuous interest due to their varied biological activity. In order to overcome one of their major drawbacks, the low solubility, various encapsulation methods have been intensively studied. In this paper, nine natural polysaccharides have been investigated as possible nanocarriers for some terpene alcohols. Prior to the molecular docking study, the alcohols have been characterized by means of the global reactivity descriptors like HOMO-LUMO gap, chemical potential and electrophilicity; also, their radical-scavenging ability has been evaluated by means of two thermodynamic parameters, BDE (Bond Dissociation Energy) and IP (Ionization Potential). The results of the molecular docking study showed that best results have been obtained for inulin (among the polysaccharides) and terpineol (among the alcohols).

***Keywords*:** terpenoids; alcohols; polysaccharides; molecular docking.

1. Introduction

Essential oils are volatile substances extracted from different parts of plants: flowers, buds, stems, leaves, seeds, fruits or bark. They are produced as secondary metabolites and show antibacterial, antifungal, insecticidal and antiviral properties [1, 2]. In this regard, essential oils are considered an important raw material in various fields such as the cosmetics and pharmaceutical industry [3, 4].

Their biologic activity is mainly due to the presence of terpenes, phenols and aldehydes. Often, the properties of the essential oils are rather attributed to a combination of these components than to a single compound or class of compounds [5, 6].

The main alcohols with terpenoid structure are citronellol, linalool, nerol, lavandulol, geraniol and terpineol. The applications of the essential oils are limited due to drawbacks as low water solubility, increased volatility and strong odor [7]. In order to overcome these disadvantages, the essential oils can be encapsulated without losing their stability and functional properties [8-10]. Various natural compounds are suitable for the encapsulation; for example, gelatin and xanthan gum [11] are widely used in techniques like complex coacervation and spray drying [12, 13], alginate and inulin [14] in spray drying [15], starch and chitosan [16] in complex coacervation.

The main advantages of natural polysaccharides as delivery systems are their affordability, abundance, safety and functionality [17]. According to the same study [17], the delivery systems based on natural polysaccharides are characterized by an enhanced water dispersibility and stability. Other important properties are the safety, lack of toxicity and biodegradability. Within the present study, various polysaccharides from natural, plant and algae sources have been investigated. Cellulose is one of the natural polysaccharides from plant source and has a number of applications in the pharmaceutical and medical industries, especially the microcrystalline cellulose: diluent or binder in tablet formulation [18]. Starch, another natural polysaccharide, is widely used as binder, thickening or gelling agent. Inulin is one of the natural polysaccharide with hydrophilic character and good thermal stability [19]. It also has a number of biological functions such as prebiotic or antioxidant effect. It is used in the pharmaceutical field as stabilizer for various drugs [19]. Also, four polysaccharides from animal source have been investigated in the present study: hyaluronic acid, chitosan, xanthan gum and levan. The hyaluronic acid has applications in tissue engineering and wound healing. Its main properties are the increased biocompatibility, cell viability and regenerative ability [18]. Chitosan has the advantage of a wide range of physico-chemical properties of semi-crystalline nature [20]. Xanthan gum, a polysaccharide mainly synthesized by the gram-negative bacteria *X. campestris* has various applications as drug delivery system [21],

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while levan is mostly used as hydrogel or films for colon-targeted drugs [22].

Together with the plant and animal source polysaccharides, two natural compouds from algae source have been investigated: alginate and carrageenan. Alginate, the salt of alginic acid, is mostly obtained from brown algae. It is employed as nanoparticles or hydrogels in various drug-delivery systems [23]. Carrageenan is mostly used for the tissue regeneration and delivery system for various medications [24].

A recent study [25] describes a delivery system consisting in linalool/encapsulated alginate microspheres, used as anti-virulence target against wound infections. Also, linalool-loaded calcium-alginate biocapsules were investigated in terms of antibacterial activity against *E. coli* [26]. The results reported that the antibacterial efficiency is directly proportional to the amount of encapsulated alcohol [26]. Another delivery system consisting in linalool encapsulated into chitosan has shown good results against fungal infestation and aflatoxin B1 contamination of stored rice [27]. Also, a long-lasting and highly effective insect repellent has been proposed [28]; the formulation comprises encapsulated geraniol in gelatin/arabic gum microcapsules [28]. According to another study, terpineol-loaded polymethyl methacrylate particles present gastroprotective effect on gastric injury model [29].

The structure of the alcohols that are investigated within the present study is depicted in Figure 1.

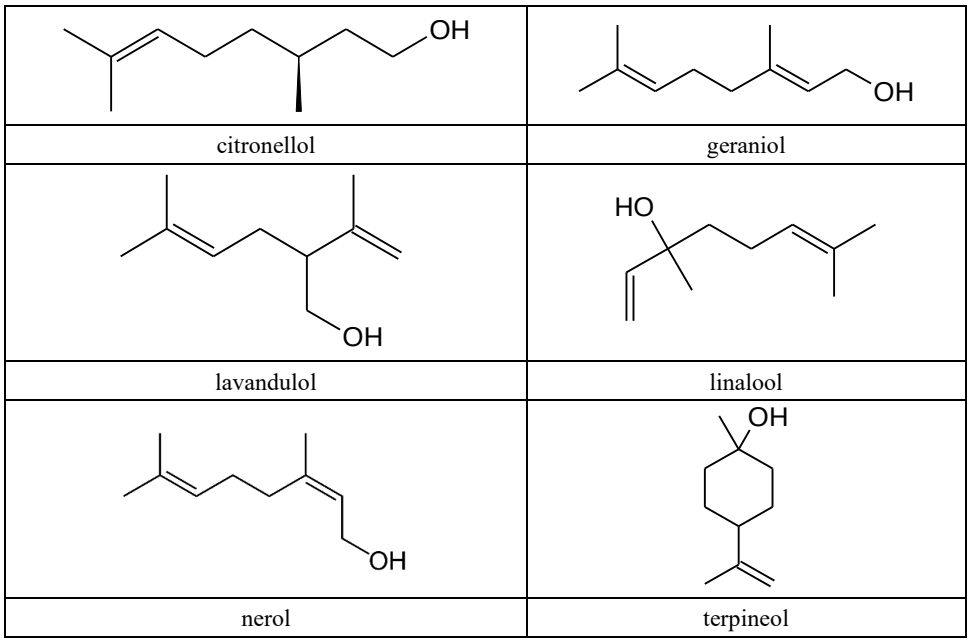

Figure 1. General structure of the investigated alcohols

The paper deals with the investigation of the interactions of the six terpene alcohols with nine natural polysaccharides from plant, animal and algae sources: inulin, pectin, starch (plant-source natural polysaccharides), chitosan, hyaluronic acid, levan, xanthan gum (animal-source natural polysaccharides), alginate and carrageenan (algae-source polysaccharides). The present study aims to evaluate, by means of computational methods, the most viable natural polysaccharide as delivery system for the terpene alcohols, prior to any experimental studies.

Prior to the molecular docking, geometry optimization of the six ligands together with the computations of some global reactivity descriptors have been performed. Also, the distribution of the frontier molecular orbitals is discussed and two important thermodynamic parameters, BDE (bond dissociation enthalpy) and IP (ionization potential), have been computed in order to characterize the radical-scavenging activity of the hydroxyl groups. The best conformation of each terpene alcohols will be *in silico* tested for the evaluation of the antimicrobial activity, by molecular docking against the crystal structure of *E. coli* FabH.

2. Computational details

Geometry optimization and vibrational analysis of the six alcohols were performed at B3LYP/6-311++G level of theory with Gaussian 09W software [30]; the results have confirmed that the obtained structures are true minima. The corresponding radicals and cation radical of the alcohols have been obtained from the initial optimized structures; a subsequent geometry optimization and vibrational analysis has been performed at B3LYP/6-311G level of theory, followed by a single-point computation using the 6-311++G basis set. In order to avoid issues regarding the spin contamination, restricted open-shell (ROB3LYP) computations have been performed for all the radical species.

Chem3D software has been employed for the computation of molecular shape descriptors: ovality, Connolly accessible area, Connolly solvent excluded volume and for the partition coefficient logP. Ovality represents the approximation of the deviation degree from the spheric shape. Connolly accessible area is considered as the surface of the compound that is accessible to the solvent; Connolly solvent-excluded volume is the sum of both van der Waals and interstitial

volumes [31]. Autodock Vina [32] has been employed for the docking simulation. The polysaccharides were assigned as receptors and a grid box of 40x40x40 Å was used, the center of the grid box being considered the center of the polysachharides. The optimized structures of the alcohols were loaded as ligands and the torsions along the rotatable bonds were assigned. The visualization of the results was also performed by means of AutoDock Vina software [32]. The antimicrobial activity of the terpene alcohols has also been evaluated with AutoDock Vina; the best conformation of the alcohols with each nanocarrier was loaded as ligand, and the crystal structure of *E. coli* FabH [33] was assigned as receptor. In order to perform the molecular docking [34, 35], the following procedure has been performed: the water molecules from the receptor structure have been removed, together with the non-polar hydrogen atoms. The total charge was computed and the crystal structure of *E. coli* FabH was assigned as receptor. Also, a grid box of 40x40x40 Å was employed, the center of the grid box being considered the center of the *E. coli* crystal structure.

3. Results and discussion

3.1. Characterization of the terpene alcohols: global descriptors of reactivity, radical-scavenging ability

The energies of the frontier molecular orbitals HOMO and LUMO (see Table 1), computed for each optimized structure, have been employed for the calculation of the global reactivity descriptors. Chemical hardness is a measure of resistance to charge transfer, while the electrophilicity is a measure of the tendency to attract electrons in a chemical bond and is defined as the opposite of chemical potential. The global reactivity descriptor values are depicted in Table 2. The results confirm that the monoterpene alcohols prefer to act as an electron donor rather than an electron acceptor. The smallest values of the chemical potential and electrophilicity have been obtained for citronellol, compound that has a single carbon-carbon double bond.

Table 1. Energies of the frontier molecular orbitals HOMO and LUMO (B3LYP/6-311G)

Compound	E_{HOMO} (a.u.)	E_{LUMO} (a.u.)	HL gap (eV)
Citronellol	-0.233	0.0250	7.02
Geraniol	-0.232	0.0070	6.50
Lavandulol	-0.239	-0.0005	6.49
Linalool	-0.237	0.0025	6.51
Nerol	-0.235	-0.0003	6.38
Terpineol	-0.252	0.0122	7.19

Table 2. Global descriptors of reactivity (B3LYP/6-311G)

Compound	Chemical potential (eV)	Electrophilicity (eV)
Citronellol	-2.83	1.14
Geraniol	-3.06	1.44
Lavandulol	-3.26	1.64
Linalool	-3.19	1.56
Nerol	-3.19	1.61
Terpineol	-3.26	1.48

Concerning the distribution of the frontier molecular orbitals, the HOMO orbitals are mainly located on both the hydroxyl group and carbon skeleton (with the exception of terpineol and citronellol, where the HOMO orbitals are not localized at the hydroxyl group), while LUMO orbitals are found on the carbon skeleton. Significant delocalization of the HOMO orbitals across the entire C-atom backbone and hydroxyl group was obtained for geraniol, lavandulol and nerol. On the other hand, LUMO orbitals are located on the carbon-carbon double bonds and on the methyl groups.

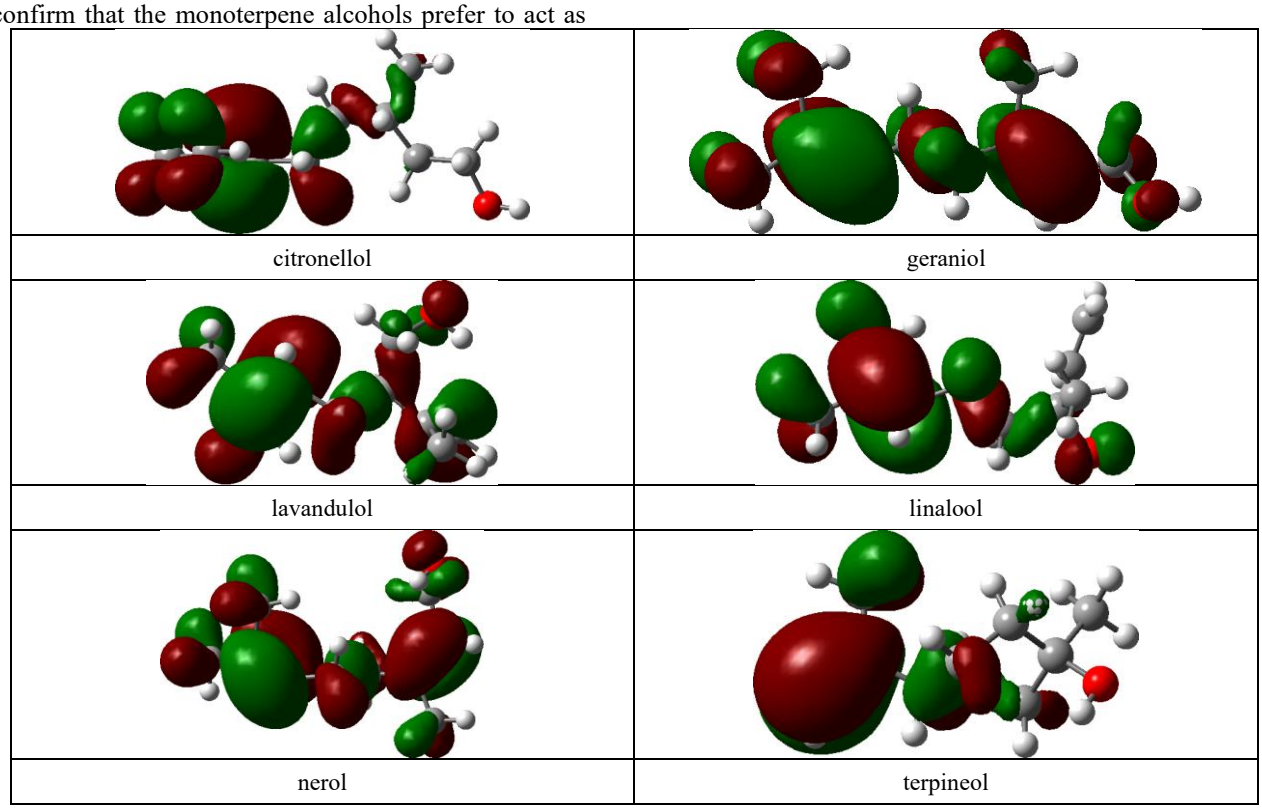

Figure 2. Graphic representation of the HOMO orbitals of the investigated terpene alcohols

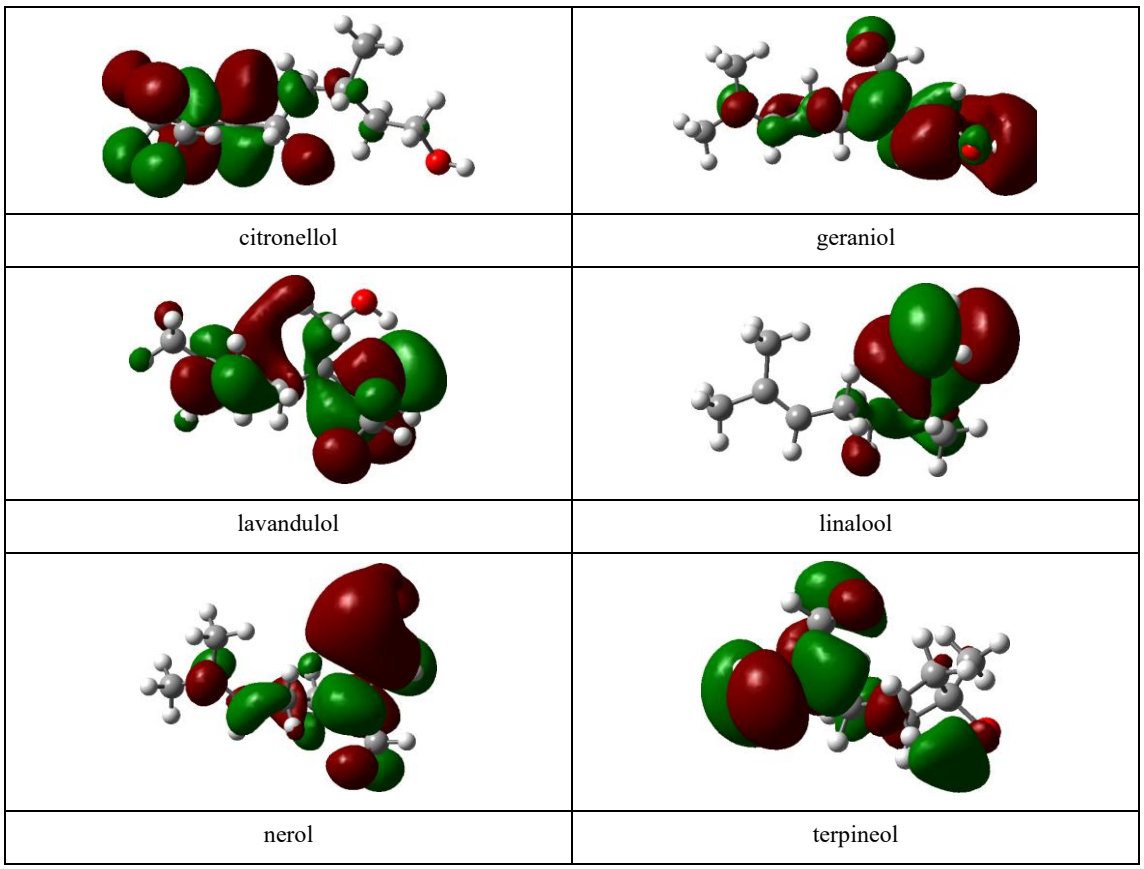

Figure 3. Graphic representation of the LUMO orbitals of the investigated terpene alcohols

The highest energy of the HOMO orbitals has been obtained for terpineol, compound characterized by the highest HOMO-LUMO gap within the series. The graphic representation of the frontier molecular orbitals is depicted in Figures 2-3.

The radical-scavenging activity of the hydroxyl group of each alcohol has been evaluated through the computation of BDE (Bond Dissociation Enthalpy), IP (Ionization Potential) and spin density. The only significant difference concerns the terpineol (the cyclic alcohol), that shows the lowest IP value among the investigated compounds and thus the higher radical-scavening ability. The results of the experimental studies outlined similar antioxidant activity for linalool and α-terpinol measured by FRAP method [36] and a slight increase antioxidant activity of linalool compared to terpinol when the DPPH assay was employed [36]. Another study [37] led to the following hierarchy of antioxidant potential measured by DPPH method: nerol>geraniol>terpineol>linalool and reducing power assay: nerol>terpineol>geraniol>linalool.

Table 3. Computed energies (B3LYP/6-311G) of the six alcohols, together with their radical and radical cation form

Compound	Radical (R·) (a.u.)	Radical cation (R^{+}·) (a.u.)	Neutral compound (a.u.)
Citronellol	-467.639	-467.998	-468.305
Geraniol	-466.412	-466.782	-468.305
Lavandulol	-466.413	-466.773	-467.079
Linalool	-466.415	-466.771	-467.077
Nerol	-466.417	-466.787	-467.080
Terpineol	-466.432	-466.773	-467.097

3.2. Molecular docking studies

Prior to the molecular docking studies, a short characterization of the steric properties of the six terpene alcohols has been performed.

The compounds with smaller areas accessible to the solvent, as well as the lowest value of ovality are terpineol, followed by lavandulol and nerol. The polar surface area has identical values for all the six alcohols, and the partition coefficient value suggest a similar lipophilic character.

Table 5. Steric characterization of the ligands: Connolly Accessible Area (CAA), Connolly Solvent-Excluded Volume (CSEV) and ovality

Compound	CAA ($Å^2$)	CSEV ($Å^3$)	Ovality
Citronellol	429.98	177.02	1.370
Geraniol	425.48	167.02	1.398
Lavandulol	400.33	172.63	1.303
Linalool	429.08	177.02	1.370
Nerol	400.33	172.63	1.303
Terpineol	370.71	168.17	1.223

Table 6. Characterization of the ligands (optimized structures)

Compound	Polar surface area (Å^2)	logP
Citronellol	20.23	2.799
Geraniol	20.23	2.515
Lavandulol	20.23	2.185
Linalool	20.23	2.295
Nerol	20.23	2.515
Terpineol	20.23	2.522

The steric parameters of each alcohol were recalculated for the best ligand conformation obtained within the docking studies on the nine polysaccharides. The results show that the best results have been obtained for terpineol, the only cyclic compound within the series, followed by geraniol, linalool and nerol. A common feature of the best ligand conformation of geraniol, linalool and nerol is a boat-like structure, whereas citronellol and lavandulol are characterized by a chair-like structure. Also, for six polysaccharides (alginate, chitosan, hyaluronic acid, inulin, starch and xanthan gum) best docking affinities have been obtained for the terpineol, geraniol and nerol (cyclic and boat-like conformation).

Table 7. Calculated binding affinities of the terpene alcohols to alginate, carrageenan and chitosan* (kcal/mol)

Terpene alcohol	Alginate	Carrageenan	Chitosan
Citronellol	-1.9/*-2.2*	-2.5/*-2.7*	-3.1/*-3.3*
Geraniol	-2.0/*-2.2*	-2.5/*-2.7*	-3.4/*-3.6*
Lavandulol	-1.9/*-2.2*	-2.4/*-2.5*	-3.0/*-3.2*
Linalool	-2.1/*-2.2*	-2.4/*-2.6*	-3.3/*-3.6*
Nerol	-2.0/*-2.1*	-2.1/*-2.5*	-3.3/*-3.5*
Terpineol	-2.4/*-2.6*	-2.9/*-3.1*	-3.5/*-3.7*

*(left- mean value obtained for the nine conformation; right (italics) – best binding value obtained for each compound)

Table 8. Calculated binding affinities of the terpene alcohols to hyaluronic acid, inulin and levan* (kcal/mol)

Terpene alcohol	Hyaluronic acid (HA)	Inulin	Levan
Citronellol	-2.1/*-2.2*	-5.6/*-6.1*	-1.8/*-2.1*
Geraniol	-2.4/*-2.5*	-5.8/*-6.0*	-1.9/*-2.1*
Lavandulol	-2.3/*-2.6*	-5.5/*-5.7*	-1.8/*-1.8*
Linalool	-2.2/*-2.5*	-5.8/*-6.0*	-1.7/*-1.8*
Nerol	-2.6/*-2.7*	-5.8/*-6.2*	-1.7/*-1.8*
Terpineol	-2.7/*-2.9*	-5.8/*-6.0*	-2.1/*-2.3*

*(left- mean value obtained for the nine conformation; right (italics) – best binding value obtained for each compound)

Table 9. Calculated binding affinities of the terpene alcohols to pectin, starch and xanthan gum*

Terpene alcohol	Pectin	Starch	Xanthan gum (XG)
Citronellol	-2.1/*-2.2*	-2.0/*-2.1*	-2.5/*-2.7*
Geraniol	-2.2/*-2.3*	-2.2/*-2.6*	-2.6/*-2.8*
Lavandulol	-2.5/*-2.6*	-2.0/*-2.2*	-2.4/*-2.5*
Linalool	-2.1/*-2.2*	-2.2/*-2.4*	-2.8/*-3.1*
Nerol	-2.4/*-2.6*	-1.9/*-2.0*	-2.3/*-2.5*
Terpineol	-2.6/*-2.7*	-2.4/*-2.5*	-2.8/*-3.1*

*(left- mean value obtained for the nine conformation; right (italics) – best binding value obtained for each compound)

It has been also observed that the higher binding affinities are not directly influenced by the number of hydrogen bonds. It can be said that the species that showed lesser interactions of close contact are the ones with lowest binding affinities. The higher values obtained for inulin may be attributed to the large surface of the polysaccharide, which led to a higher number of atoms in close contact.

The steric parameters of each alcohol - recalculated for the best ligand conformation obtained within the docking studies - together with the interactions between alcohol and polysaccharide, are discussed below. The interactions among the alcohols and polysaccharides are presented in the Supplementary file.

Table 10. Computed steric parameters for the best ligand conformations (in interactions with **alginate**)

Compound	CAA (Å^2)	CSEV (Å^3)	Ovality
Citronellol	351.218	118.583	1.341
Geraniol	346.965	116.746	1.346
Lavandulol	336.958	119.680	1.289
Linalool	338.580	122.123	1.292
Nerol	341.114	121.642	1.305
Terpineol	*320.324*	*116.444*	*1.251*

Best results have been obtained for terpineol, compound that has the lowest Connolly accessible area (CAA) and ovality values. No significant differences appear among the other five terpene alcohols. Two hydrogen bonds have been observed for citronellol (1.985 Å and 2.110 Å) and terpineol (2.197 Å and 2.084 Å); a single hydrogen bond has been formed between linalool and alginate (2.207 Å) and nerol and alginate, respectively (2.183 Å).

Table 11. Computed steric parameters for the best ligand conformations (in interactions with **carrageenan**)

Compound	CAA (Å^2)	CSEV (Å^3)	Ovality
Citronellol	364.818	117.831	1.387
Geraniol	343.385	120.843	1.312
Lavandulol	335.043	120.274	1.279
Linalool	325.076	124.502	1.230
Nerol	342.399	121.935	1.309
Terpineol	*323.240*	*117.018*	*1.248*

All the investigated terpinols establish hydrogen bonds with the polysaccharide carrageenan; two stronger intermolecular bonds of 2.017 Å (citronellol) and 1.919 Å (lavandulol) and weaker hydrogen bonds for geraniol (2.965 Å), linalool (2.852Å and 2.775 Å), nerol (2.955 Å) and terpineol (3.054 Å).

Table 12. Computed steric parameters for the best ligand conformations (in interactions with **chitosan**)

Compound	CAA (Å^2)	CSEV (Å^3)	Ovality
Citronellol	354.270	121.304	1.343
Geraniol	355.755	115.650	1.376
Lavandulol	337.398	120.470	1.291
Linalool	343.733	120.507	1.313
Nerol	355.965	118.958	1.367
Terpineol	*319.991*	*115.281*	*1.256*

Only two terpinols have formed hydrogen bonds: citronellol (2.221 Å) and geraniol (2.185 Å), the latter showing the second best binding affinity (after terpineol).

The analysis of the interactions between hyaluronic acid and the terpenoid alcohols show the formation of

hydrogen bonds for citronellol (1.926 Å and 1.962 Å), geraniol (2.114 Å), lavandulol (2.002 Å and 2.006 Å) and nerol (2.193 Å). The weaker hydrogen bonds formed by geraniol, lavandulol and nerol are correlated to larger binding affinities for these compouds (as presented in Table 8).

Table 13. Computed steric parameters for the best ligand conformations (in interactions with **hyaluronic acid**)

Compound	CAA ($Å^2$)	CSEV ($Å^3$)	Ovality
Citronellol	340.225	120.520	1.296
Geraniol	344.050	119.575	1.325
Lavandulol	343.356	119.778	1.312
Linalool	327.111	123.746	1.239
Nerol	359.641	118.690	1.371
Terpineol	*319.536*	*116.009*	*1.250*

Table 14. Computed steric parameters for the best ligand conformations (in interactions with **inulin**)

Compound	CAA ($Å^2$)	CSEV ($Å^3$)	Ovality
Citronellol	365.885	117.729	1.390
Geraniol	354.382	116.015	1.360
Lavandulol	357.120	115.934	1.373
Linalool	355.988	118.029	1.358
Nerol	360.421	115.954	1.385
Terpineol	*319.615*	*115.887*	*1.251*

According to the presented results of the docking affinities, best results among the natural polysaccharides have been obtained for inulin. The interactions alcohols-inulin are characterized by a single hydrogen bond for geraniol (1.968Å) and by the highest number of atoms in close-contact.

Table 15. Computed steric parameters for the best ligand conformations (in interactions with **levan**)

Compound	CAA ($Å^2$)	CSEV ($Å^3$)	Ovality
Citronellol	352.186	120.419	1.335
Geraniol	350.474	116.398	1.355
Lavandulol	334.174	120.597	1.281
Linalool	326.538	124.700	1.231
Nerol	340.325	123.242	1.288
Terpineol	*321.343*	*115.727*	*1.258*

The analysis of the interactions among levan and alcohols outlined the smallest number of atoms in close contact; hydrogen bonds have been formed in the case of citronellol (2.167 Å), lavandulol (2.113 Å), linalool (2.218 Å), nerol (1.885Å) and terpineol (2.043 Å).

Three terpene alcohols form hydrogen bonds with pectin: citronellol (1.790Å and 2.248Å), linalool (1.939Å), and terpineol (2.238Å). Best binding affinity has been obtained for terpineol, compound with the smallest Connolly accessible area, Connolly solvent-excluded volume and ovality. The values of the binding affinities for citronellol and linalool towards pectin (Table 9) suggest that they are not significantly influenced by the presence of the hydrogen bonds.

Table 16. Computed steric parameters for the best ligand conformations (in interactions with **pectin**)

Compound	CAA ($Å^2$)	CSEV ($Å^3$)	Ovality
Citronellol	343.827	122.813	1.294
Geraniol	343.461	118.302	1.339
Lavandulol	349.594	115.053	1.356
Linalool	326.009	124.453	1.233
Nerol	355.176	118.413	1.369
Terpineol	*318.985*	*115.513*	*1.252*

Table 17. Computed steric parameters for the best ligand conformations (in interactions with **starch**)

Compound	CAA ($Å^2$)	CSEV ($Å^3$)	Ovality
Citronellol	345.491	121.638	1.314
Geraniol	348.719	115.266	1.353
Lavandulol	343.006	119.902	1.311
Linalool	338.783	121.170	1.303
Nerol	325.939	125.130	1.248
Terpineol	*323.699*	*116.883*	*1.249*

As regards the interactions alcohols-starch., a single hydrogen bond is established between geraniol and starch (2.206Å).

Table 18. Computed steric parameters for the best ligand conformations (in interactions with **xanthan gum**)

Compound	CAA ($Å^2$)	CSEV ($Å^3$)	Ovality
Citronellol	362.043	117.463	1.379
Geraniol	347.459	116.623	1.339
Lavandulol	339.508	121.214	1.299
Linalool	338.314	121.986	1.283
Nerol	340.565	122.474	1.290
Terpineol	*320.844*	*116.627*	*1.247*

Hydrogen bonds have been formed among xanthan gum and citronellol (2.052Å), lavandulol (2.238Å), linalool (2.075Å) and terpineol (2.117Å), respectively.

The antimicrobial activity of the above-characterized best conformation of the alcohols (from the interactions with each polysaccharide) was investigated by molecular docking to the crystal structure of *E. coli*. The results are presented in Table 19 and suggest a stronger antimicrobial behavior for geraniol (with Xantham Gum as nanocarrier) and terpineol (same results have been obtained for three nanocarriers: chitosan, pectin and starch).

Table 19. Calculated binding affinities* of the best conformation of terpene alcohols towards *E. coli* FabH (1hnj.pdb) (kcal/mol)

	Citronellol	Geraniol	Lavandulol	Linalool	Nerol	Terpineol
Alginate	-4.14	-4.17	-4.12	-4.11	-3.95	-4.90
Carrageenan	-4.12	-4.41	-4.00	**-4.34**	-4.21	-4.95
Chitosan	-3.98	-4.44	-4.16	-3.96	-4.21	**-4.96**
Hyaluronic acid	-4.17	-4.26	-4.15	-4.22	**-4.46**	-4.94
Inulin	-4.04	-4.41	-4.13	-4.21	-4.27	-4.81
Levan	**-4.30**	-4.32	-4.03	-4.07	-4.13	-4.87
Pectin	-4.11	-4.45	-4.23	-4.25	-3.93	**-4.96**
Starch	-3.90	-4.14	-4.16	-4.16	-4.12	**-4.96**

	Citronellol	Geraniol	Lavandulol	Linalool	Nerol	Terpineol
Xantham Gum	-4.23	**-4.97**	**-4.27**	-4.27	-4.18	-4.94

* mean values of the nine docked conformations

4. Conclusions

The present paper aimed to evaluate both the radical-scavenging activity and the possibility of encapsulation in natural polymers of some non-phenolic antioxidants found in essential oils. In this regard, a series of six compounds with monoterpene structure were investigated, namely citronellol, geraniol, lavandulol, linalool, nerol and terpineol.

The results of the study showed that a more pronounced stability (conferred by a higher value of the HOMO-LUMO gap) was obtained for terpineol, the alcohol with cyclic structure. The graphic representation of the frontier molecular orbitals underlines their location on the carbon atom skeleton (LUMO orbitals) and on both hydroxyl group and carbon skeleton for geraniol, nerol, linalool and lavandulol (HOMO orbitals).

The computation of the thermodynamic parameter BDE led to higher values compared with the corresponding ones for phenolic OH groups (around 89 kcal/mol [38]), which suggests a weaker radical-scavenging activity.

The aim of the study was to estimate, prior to experimental studies, if the natural polysaccharides can be suitable carriers for the terpene alcohols. Among the considered receptor compounds, best results have been obtained for inulin. The molecular docking of the six monoterpene derivatives using natural polymers as targets led to favorable results for terpineol, followed by geraniol and lavandulol. The interactions that determined the aforementioned results are mostly due to the atoms in close contact, followed by the formation of hydrogen bonds. The steric characterization of the best conformation of terpineol, regardless the polysaccharide receptor, show similar results for the Connolly Accessible Area, Connolly Solvent-Excluded Volume and ovality, namely ~320 $Å^2$, ~116 $Å^3$ and ~ 1.250.

The last part of the study investigated the antimicrobial activity of the six terpene alcohols, using the best conformations obtained from the interactions with the natural polysaccharides. A stronger antimicrobial activity has been obtained for geraniol (structure with Xantham Gum as nanocarrier) and terpineol (for the structures corresponding to the encapsulation in chitosan, pectin and starch).

Conflict of interest

The authors declare that there is no conflict of interest concerning the publication of this research article.

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