Simulation of the degradation of the main constituent from Lavandula dentata L. essential oil

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Research Article

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Abstract

The demand for essential oils is growing every year as an alternative to artificial additives. *Lavandula dentata* L. is a species of lavender that has acclimatized in Brazil and its oil has pharmacological and biological properties that give it great commercial importance. In this context, the market for essential oils has been promising and, therefore, a study into the degradation of these products interferes with the quality and biological activity of these oils, making it extremely important for their preservation. The aim of this study was to simulate the reaction equilibrium of the degradation of the main constituent from *Lavandula dentata* L., Lamiaceae, essential oil, 1,8-cineole (1), using the Aspen Plus® simulator v. 12 in an equilibrium reactor at a temperature of 30°C and a pressure of 1 atm. The results of the simulations indicated that ketones are the major oxidation products of 1,8-cineole when compared to the alcohols 1,3,3-trimethyl-2-oxabicyclo-[2.2.2]-octan-5-ol (2) and 1,3,3-trimethyl-2-oxabicyclo-[2.2.2]-octan-6-ol (3). In addition, the ketone 1,3,3-trimethyl-2-oxabicyclo-[2.2.2]-octan-6-one (5) was formed with a molar flow rate 1.5 times greater than the ketone 1,3,3-trimethyl-2-oxabicyclo-[2.2.2]-octan-5-one (4) due to the lower steric hindrance. Sensitivity analyses were carried out for the simulations studied, which led to the conclusion that the formation of alcohols and ketones was favored by increasing the molar oxygen flow rate. On the other hand, increasing the temperature favored the formation of ketone (5) and decreased the formation of ketone (4).

INTRODUCTION

The international market for essential oils is showing a steady growth trend due to the increased consumption of natural products to replace synthetic additives (Bizzo and Rezende 2022). According to the Ministry of Industry, Foreign Trade and Services of the Brazilian Federal Government, in 2023 Brazilian exports of essential oils, perfume and flavor materials were 14.2% higher than in 2022, with revenues of US$ 566.92 million, which placed Brazil 71st in the ranking of total exports in this segment (Brazil 2023).

Essential oils are complex mixtures of volatile, lipophilic, odoriferous and liquid substances. They are synthesized by plant species during their secondary metabolism with the aim of protecting, conserving and reproducing these species (Alves et al. 2020, Ramos et al. 2020). Due to their biological properties, they are used as raw materials in hygiene and cleaning products, cosmetics and perfumery industries, drug production in pharmaceutical industries and food industries (Afkar 2023, Silva 2018; Silva 2021).

One of the most widely used essential oils and one for which demand is increasing are oils derived from Lavender (Cruz Sanchez-Alarcos et al. 2024). *Lavandula dentata* L. is the lavender species that has acclimatized best in Brazil and can be found in regions of Minas Gerais, São Paulo and southern Brazil (Reis et al. 2022, Martins et al. 2019, Justus et al. 2018). This plant has medicinal and therapeutic properties that are related to the presence of the oxygenated monoterpenes, 1,8-cineole and camphor, attributing to it antifungal, antispasmodic and bactericidal action (Martins et al. 2019, Masetto et al. 2011, Abdali et al. 2022, Jilali et al. 2023).

Studies on the essential oil of *Lavandula dentata* L. grown in Brazil, obtained by hydrodistillation, have indicated that the chemical composition of the oil corresponds to 92% monoterpenoids and 2% sesquiterpenoids, with the main constituent being the monoterpene 1,8-cineole (Bruno and Almeida 2021; Martins et al. 2019; Justus et al. 2018).

In the presence of oxygen, light, heat and humidity, essential oils are very unstable and undergo numerous degradation reactions that make their conservation difficult (Guimarães et al. 2008). These changes occur mainly due to oxidation and polymerization reactions (Simões et al., 2004).

Temperature can influence the stability of essential oils since, in general, chemical reactions accelerate with increasing heat due to the dependence of temperature on the reaction rate (Turek and Stintzing 2013). In addition, organic substances in the presence of energy (through heating or light irradiation) can generate free radicals as a result of the homolytic cleavage of chemical bonds, causing the acceleration of auto-oxidative processes and the formation, when they react with the oxygen present in the air, of peroxides and hydroperoxides, which are unstable compounds capable of generating new, even more reactive radicals (Guimarães et al. 2008).

The most common degradation products of 1,8-cineole come from oxidation reactions, reactions of this compound with oxygen gas, for example. 1,8-cineole (eucalyptol or 1,3,3-trimethyl-2-oxabicyclo[2.2.2]octane), shown in Fig. 1, is an oxabicycle whose oxidation products can be alcohols or ketones.

The study by Farlow et al. (2013) showed the formation of alcohol 3 from the oxidation of 1,8-cineole using an oxidative hemoprotein called Cytochromes P450, isolated from a bacterium, as a catalyst. Slessor et al. (2010), in turn, believe that this hemoprotein metabolizes 1,8-cineole in two stages: first with hydroxylation at carbon 6, obtaining the alcohol, followed by oxidation of this alcohol to form the ketone.

The oxidation of 1,8-cineole with the formation of a ketone is also corroborated by the study by Imwinkelried et al. (2020), which evaluated the formation of ketones 4 and 5 in a radical reaction of 1,8-cineole with atomic chlorine at 298 degrees Kelvin.

Ceacero-Veja et al. (2011) observed the formation of ketones as the majority of oxidation products through a study of daytime oxidation reactions of 1,8-cineole at a temperature of 25°C and a pressure of 0.97 atm. The oxidation products were obtained via radical reactions starting from chlorine atoms or hydroxyl radicals.

This study will evaluate the formation of mild and vigorous oxidation products, alcohols and ketones respectively, of 1,8-cineole, the main constituent of *Lavandula dentata* L. essential oil, using the Aspen Plus® process simulator.

Aspen Plus® is a simulator that uses mathematical models to reproduce processes in an industrial plant, equipment or reaction system (Souza 2017; Oliveira et al. 2017). In addition, according to Cruz

Sanchez-Alarcos et al. (2024) Aspen Plus® can be used as an important tool to estimate the physical properties and binary interaction parameters when evaluating the equilibrium of the lavender essential oil extraction system with a supercritical fluid.

METHODOLOGY

To simulate the degradation process of *Lavandula dentata* L. essential oil, using Aspen Plus® v. 12 software, the formation of oxidation products of the main constituent, 1,8-cineole, was evaluated in three simulations. A mild oxidation reaction was proposed with the formation of a mixture of alcohols 2 and 3 and a vigorous oxidation reaction with the formation of ketones 4 and 5 using 1,8-cineole and oxygen gas as reactants.

Figure 2 shows the general oxidation reaction of 1,8-cineole and Table 1 shows the IUPAC (International Union of Pure and Applied Chemistry) nomenclature of the possible products according to functional group and position in the molecule.

Table 1
IUPAC nomenclature for the oxidation products of 1,8-cineole.

	R	**Product**
Mild oxidation reaction	OH (5 Position)	1,3,3-trimethyl-2-oxabicyclo-[2.2.2]-octan-5-ol (2)
	OH (6 Position)	1,3,3-trimethyl-2-oxabicyclo-[2.2.2]-octan-6-ol (3)
Powerful oxidation reaction	C = O (5 Position)	1,3,3-trimethyl-2-oxabicyclo-[2.2.2]-octan-5-ona (4)
	C = O (6 Position)	1,3,3-trimethyl-2-oxabicyclo-[2.2.2]-octan-6-ona (5)

The first simulation aimed to evaluate mild oxidation, with the formation of alcohols, and in the second simulation, the formation of ketones from energetic oxidation. The third simulation evaluated the formation of alcohols and ketones as oxidation products of 1,8-cineole under the previously determined conditions.

In the Aspen Plus® simulator, the modeling of a system begins with the specification of its properties. At this stage, the chemical components included in the system and the thermodynamic model used to calculate the properties were defined (Souza 2017).

The thermodynamic model chosen was NRTL (Non-Randon Two-Liquid). This choice was made due to the formation of a polar, non-electrolytic mixture from the 1,8-cineole oxidation reaction. In addition, this model is suitable for systems with a pressure range of less than 10 bar (Souza 2017).

To structure the reaction system, a Gibbs reactor was chosen, which uses the principle of minimizing Gibbs free energy to obtain the concentrations of each component when the reaction reaches equilibrium (Oliveira 2017).

This reactor had continuous flow conditions and was fed by an input stream at a temperature of 30°C and a pressure of 1 atm, with a molar flow rate of 50 kmol.h^{-1} of 1,8-cineole and 50 kmol.h^{-1} of oxygen. These molar flow rate, temperature and pressure specifications were the same for all three simulations. In addition, the Gibbs reactor was operated at a pressure of 1 atm and a temperature of 30°C.

Figure 3 shows the structure of the simulation of the reaction system studied and the molar flow rates of the Gibbs reactor inlet stream, represented by block B1 in the Aspen Plus® simulator.

In addition, the influence of temperature and oxygen molar flow rate on the formation of the oxidation products of 1,8-cineole were evaluated, and two sensitivity analyses were carried out for each simulation.

The specifications of the variables manipulated for each of the two analyses are shown in Table 2. It is important to note that the increment corresponds to the value at which the manipulated variable will be analyzed within the specified interval, starting from the initial value to the final value, resulting in a number of points for the simulator to analyze the system.

Table 2
Specifications of the variables manipulated for the sensitivity analyses.

	First analysis	**Second analysis**
Manipulated variable	Temperature	Oxygen molar flow rate
Type	Block-var	Molar flow
Location	Bloco B1	Input current
Unit	°C	kmol.h^{-1}
Initial value	20°C	0 kmol.h^{-1}
Final value	35°C	55 kmol.h^{-1}
Increase	5°C	5 kmol.h^{-1}

The specifications presented for the manipulated variables, temperature and molar oxygen flow rate, in the two sensitivity analyses were the same for the three simulations.

RESULTS AND DISCUSSIONS

Table 3 shows the results obtained for the three simulations studied, evaluating mild oxidation with the formation of alcohols, energetic oxidation with the formation of ketones, and oxidation evaluating the reaction equilibrium with the formation of the four products.

Table 3
Results of three simulations of the 1,8-cineole oxidation.

		Simulation evaluating the formation of alcohols	**Simulation evaluating the formation of ketones**	**Simulation evaluating the formation of alcohols and ketones**
	Input current	**Output current**		
	Molar flow rates (kmol.h^{-1})			
Oxygen	50	25	0	0
1,8-cineole	50	0	0	0
Alcohol 2	0	25	-	0
Alcohol 3	0	25	-	0
Ketone 4	0	-	19,94	19,94
Ketone 5	0	-	30,06	30,06
Water	0	0	50	50
Mass flow rates **(kg.h^{-1})**	9312,56	9312,56		
Temperature (°C)	30	30		
Pressure (atm)	1	1		
Vapor fraction	0,50	0		
Liquid fraction	0,50	1		

Formation of alcohols as oxidation products

The results in Table 3 shows that when 1,8-cineole was reacted with oxygen gas under conditions of 30°C and 1 atm in a reaction with a 2:1 molar ratio of 1,8-cineole and oxygen gas, a mixture was formed in the liquid phase of alcohols 2 and 3 at the same molar flow rate. In this context, 25 kmol.h^{-1} of each of the alcohols was formed and no water was formed.

Ceacero-Veja et al. (2011) carried out a study on the radical oxidation reactions of 1,8-cineole using chlorine atoms or hydroxyl radicals as an initiator under atmospheric conditions, at a temperature of

25ºC and a pressure of 0.97 atm, applying ultraviolet radiation for 1200 seconds. In this context, the results obtained for the chlorine/1,8-cineole/air mixture using the Gas Chromatography technique coupled to a Flame Ionization Detector (GC-FID) showed the formation of alcohols 2 and 3 in similar proportions.

From the results obtained, it was possible to observe that the simulation of the oxidation of 1,8-cineole with the formation of alcohols as products is similar to that shown in the study by Ceacero-Veja et al. (2011).

Figure 4 shows the three-dimensional representation of the molecules of alcohols 2 and 3 using the Chem3D Pro software version 12.0.2. It can be seen that for the alcohols, the sigma bond formed between the carbon and oxygen in position 6 is less sterically hindered due to the distance between the hydroxyl and the methyl substituents on carbon 3. However, the formation of alcohol 2 is possible, although it is closer to carbon 3 and its methyl substituents. The approach of the oxygen molecule can occur through the lower plane of the 1,8-cineole molecule, since the methyl substituents on carbon 3 are on the upper plane of the molecule, causing less steric hindrance. Thus, alcohols 2 and 3 are obtained in the same proportion, as indicated by the simulation results.

Formation of ketones as energetic oxidation products

From the results shown in Table 3, it can be seen that when 1,8-cineole reacts with oxygen gas in a reaction with a stoichiometric ratio of 1:1, a mixture is formed in the liquid phase consisting of 19.94 kmol.h^{-1} of ketone 4, 30.06 kmol.h^{-1} of ketone 5 and 50 kmol.h^{-1} of water, under conditions of 30°C and 1 atm.

This result is as expected since the study carried out by Ceacero-Veja et al. (2011) on the oxidation reactions of 1,8-cineole by CG-FID showed that the chlorine/1,8-cineole/air mixture after photolysis in 1200 seconds has ketone 5 as the main oxidation product.

Figure 5 shows the three-dimensional representation of ketone molecules 4 and 5, respectively. In this case, the formation of ketone 5 is favored over ketone 4 since there is a steric hindrance due to the methyls of carbon 3, with spatial proximity to carbon 5 and formation of the double bond of the ketone carbonyl, which generates a carbon with sp^2 hybridization. Thus, ketone 5 is a less hindered oxidation product, more stable and therefore the majority.

Evaluation of the formation of alcohols and ketones as oxidation products

The results in Table 3 shows that a mixture was formed in the liquid phase consisting of 30.06 kmol.h^{-1} of ketone 5, 19.94 kmol.h^{-1} of ketone 4 and 50 kmol.h^{-1} of water.

In view of this, it was possible to conclude that the formation of ketones as oxidation products of 1,8-cineole is greater than the formation of alcohols, a result which is in line with what was shown in the study by Ceacero-Veja et al. (2011) since the chromatogram obtained by CG-FID for the chlorine/1,8-cineole/air mixture after photolysis shows that the peak referring to ketone 5 and ketone 4 have a much greater area than the peaks of the alcohols.

Sensitivity analysis - Formation of alcohols as oxidation products

Table 4 shows the result obtained for the sensitivity analysis using temperature as the manipulated variable and the molar flow rates of alcohols 2 and 3 as the response variables.

Table 4
Temperature sensitivity analysis for the simulation of 1,8-cineole oxidation with the formation of alcohols.

Analysis	Temperature (°C)	Molar Flow Rate - Alcohol 2 ($kmol.h^{-1}$)	Molar Flow Rate - Alcohol 3 ($kmol.h^{-1}$)
1	20	25	25
2	25	25	25
3	30	25	25
4	35	25	25

It was observed that the formation of the isomers of alcohols as oxidation products of 1,8-cineole was not influenced by temperature since, when the temperature was varied, the response of the molar flow rates of alcohols 2 and 3 was constant, linear. Furthermore, it was concluded that varying the temperature does not influence the majority formation of one alcohol over the other, since both are formed at the same rate of 25 $kmol.h^{-1}$, as indicated by the simulation results and the three-dimensional conformation of the molecules of the products obtained.

In addition, Fig. 6 shows the 3D surface obtained when evaluating the molar flow rate of alcohols 2 and 3, varying the temperature and the molar flow rate of oxygen. This 3D graph is the same for both alcohols since the formation of these products occurs at the same rate. It can be seen that increasing the molar flow rate of oxygen leads to an increase in the formation of products. However, as this is a reaction with a molar ratio of 2 moles of 1,8-cineole to 1 mol of oxygen, when 50 $kmol.h^{-1}$ of 1,8-cineole reacts with 25 $kmol.h^{-1}$ of oxygen, a plator is observed in view of the total consumption of the limiting reagent. On the other hand, increasing the temperature has no influence on the formation of regioisomer alcohols.

Sensitivity analysis - Formation of ketones as oxidation products

Figure 7 shows the result obtained for the sensitivity analysis using temperature as the manipulated variable and the molar flow rates of ketones 4 and 5 as the response variables.

Figure 7 shows that ketone 5, the purple curve, is the thermodynamically favored product since its molar flow rate increases as the temperature rises. On the other hand, the formation of ketone 4, the pink curve, is the kinetically favored product up to 25°C since the radicals formed in this position have a lower activation energy due to the inductive effect, donation of electronic density, of the methyls linked to carbon 3. This corroborates the analysis of the three-dimensional arrangement of the molecules of ketones 4 and 5 in Fig. 5.

Figure 8 shows the result obtained for the molar flow rate of ketone 4 and 5 when carrying out the sensitivity analysis of the oxygen molar flow rate and temperature parameters, concomitantly, in the 1,8-cineole oxidation reaction.

Looking at Fig. 8a, it can be seen that as the molar oxygen flow rate increases, the formation of ketone 4 also increases up to approximately 30 kmol.h^{-1}. On the other hand, at this point where the formation of ketone 4 is maximum, the temperature is minimum, 20°C. On the other hand, Fig. 8b shows that there is a directly proportional relationship between the two variables in the formation of ketone 5, whose maximum value of approximately 35 kmol.h^{-1} is obtained at a temperature of 35°C and under 50 kmol.h^{-1} of oxygen gas.

Therefore, from the analysis of Fig. 8a and b, it can be concluded that the formation of ketones 4 and 5 is favored by increasing the molar flow rate of oxygen. However, the formation of ketone 4 is inversely proportional to the increase in temperature and, on the other hand, the formation of ketone 5 is greater the higher the temperature.

Sensitivity analysis - Formation of alcohols and ketones as oxidation products

Figure 9 shows the results obtained for the sensitivity analyses using temperature and oxygen molar flow rate, respectively, as the manipulated variable and the molar flow rates of ketones and alcohols as the response variables.

From the analysis of Figs. 9a and b, it can be seen that as there was no formation of alcohols 2 and 3 when simulating the oxidation of 1,8-cineole with the formation of the 4 possible oxidation products, in both analyses the alcohol products overlap at the zero of each graph. In addition, the formation of ketone 5, the purple line in both graphs, is favored by an increase in temperature and an increase in the molar flow of oxygen, which is the major product of the 1,8-cineole oxidation reaction in reactions above 25°C.

FINAL CONSIDERATIONS

This study evaluated the oxidative degradation of 1,8-cineole, the main constituent of the essential oil of *Lavandula dentada* L. The analysis was carried out using the Aspen Plus® v. 12 process simulator, using a Gibbs-type reactor and the NRTL thermodynamic model.

The result of the simulation evaluating the formation of alcohols as products indicated that alcohols 2 and 3 are formed in the same proportion with the same molar flow rate. On the other hand, the simulation evaluating the formation of ketones indicated that the formation of ketone 5 is 1.5 times greater than the formation of ketone 4. The result of the simulation evaluating the formation of alcohols and ketones, in turn, led to the conclusion that there was no formation of alcohols and that ketones are the major oxidation products of 1,8-cineole.

In addition, the sensitivity analysis showed that there is no influence of temperature on the molar flow rate of the alcohols obtained. On the other hand, increasing the availability of oxygen in the reaction medium can increase the concentration of the alcohols up to the point where all the 1,8-cineole is consumed.

It was also observed from the sensitivity analysis that increasing the temperature favored the formation of ketone 5 and decreased the formation of ketone 4. In addition, it was possible to conclude that increasing the molar flow rate of oxygen also increases the formation of ketones, but there is greater formation of ketone 5.

It was therefore possible to observe that increasing the availability of oxygen also increases the degradation of essential oils by oxidation, and for lavender essential oil, ketone 5 is the major product. Therefore, safety in the storage of essential oils is of paramount importance and completely filled and hermetically sealed amber glass containers are recommended.

Abbreviations

IUPAC	International Union of Pure and Applied Chemistry
NRTL	Non-Randon Two-Liquid
GC-FID	Gas Chromatography coupled to a Flame Ionization Detector

Declarations

Conflict of interest The authors declare that there is no conflict of interest.

References

1. Afkar S (2023) Assessment of chemical compositions and antibacterial activity of the essential oil of Mentha piperita in response to salicylic acid. Natural Product Research. https://doi.org/10.1080/14786419.2023.2256020

2. Alves CCF, Oliveira JD, Estevam EBB, Xavier MN, Nicolella HD, Furtado RA, Tavares DC, Miranda MLD (2020) Antiproliferative activity of essential oils from three plants of the Brazilian Cerrado: Campomanesia adamantium (Myrtaceae), Protium ovatum (Burseraceae) and Cardiopetalum calophyllum (Annonaceae). Brazilian Journal of Biology. https://doi.org/10.1590/1519-6984.192643
3. Bizzo HR, Rezende CM (2022) The essential oil market in Brazil and worldwide over the last decade. Química Nova 45:949-958. http://dx.doi.org/10.21577/0100-4042.20170889
4. BRAZIL. Ministry of Industry, Foreign Trade and Services. 2023. Available at: https://comexstat.mdic.gov.br/pt/comex-vis/4/551
5. Bruno CMA, Almeida MR (2021) Essential and vegetable oils: Raw materials for making bioproducts in Experimental Organic Chemistry classes. Química Nova. https://doi.org/10.21577/0100-4042.20170722
6. Ceacero-Veja AA, Ballesteros B, Bejan I, Barnes I, Albaladejo J (2011) *Daytime Reactions of 1, 8-Cineole in the Troposphere*. *ChemPhysChem*. https://doi.org/10.1002/cphc.201100077
7. Cruz Sánchez-Alarcos E, Garcia MT, Gracia I, Rodriguez JF,Garcia-Vargas JM (2024) Modelling of the equilibrium of supercritical $CO_{2\,+}$ lavander essential oil with Aspen Plus®. The Journal of Supercritical Fluids. https://doi.org/10.1016/j.supflu.2024.106239
8. El Abdali, Y.; Agour, A.; Allali, A.; Bourhia, M.; El Moussaoui, A.; Eloutassi, N.; Salamatullah, A.M.; Alzahrani, A.; Ouahmane, L.; Aboul-Soud, M.A.M.; et al. *Lavandula dentata* L.: Phytochemical Analysis, Antioxidant, Antifungal and Insecticidal Activities of Its Essential Oil.Plants2022,11,311. https:// doi.org/10.3390/10.3390/ plants11030311
9. Farlow AJ, Bernhardt PV, De Voss JJ (2013) Synthesis of oxygenated cineole derivatives from cineole: utility of cytochrome P450cin as an enantioselective catalyst. **Tetrahedron: Asymmetry**. http://dx.doi.org/10.1016/j.tetasy.2013.02.004
10. Guimarães LGL, Cardoso MG, Zacaroni LM, Lima RK, Pimentel FA, Morais AR (2008) nfluence of light and temperature on the oxidation of lemongrass essential oil (*Cymbopogoncitratus* (D.C.) STAPF). Química Nova. https://doi.org/10.1590/S0100-40422008000600037
11. Imwinkelried G, Gaona-Colmán E, Teruel MA, Blanco MB (2020) Kinetics, mechanism and CH3C(O)CH3 formation in the Cl-initiated oxidation of 1,8-cineole at 298 K and atmospheric pressure. Chemical Physics Letters. https://doi.org/10.1016/j.cplett.2019.136901
12. Jilali SBE, Rachid I, Ghada B, Tarik M, Sanae R, Abderrazzak K. (2023)Effect of Isolation Techniques on the Quantity, Quality, and Antimicrobial Activity of *Lavandula dentata* Essential Oils. Tropical Journal of Natural Product Research 7(4):2713-2717 http://www.doi.org/10.26538/tjnpr/v7i4.7
13. Justus B, Almeida VP, Gonçalves MM, Assunção DPSF, Borsato DM, Arana A FM, Maia BHLNS, Paula JFP, Budel JM, Farago PV (2018) Chemical Composition and Biological Activities of The Essential Oil And Anatomical Markers Of *Lavandula Dentata* L. Cultivated In Brazil. Brazilian Archives Of Biology and Technology**.**https://doi.org/10.1590/1678-4324-2018180111
14. Martins RP, Gomes RAS, Malpass ACG, Okura MH (2019) Chemical characterization of *Lavandula dentata* L. essential oils grown in Uberaba-MG. Ciencia Rural. https://doi.org/10.1590/0103-

8478cr20180964

15. Masetto MAM, Deschamps C, Mógor AF, Bizzo HR (2011) Essential oil content and composition of *Lavandula dentata* L. inflorescences and leaves at different stages of floral development and harvest times. Brazilian Journal of Medicinal Plants. https://doi.org/10.1590/S1516-05722011000400007
16. Oliveira AFA, Queiroz PV, Cunha CHF, Sato AG, Rodrigues FA (2017) Transesterification of ethyl acetate with methanol: Thermodynamic evaluation. The Journal of Engineering and Exact Sciences. https://doi.org/10.18540/2446941602012016001
17. Ramos YJ, Felisberto JRS, Oliveira CC, Pontes ED, Machado DB, Fonseca IC, Moreira DL (2020) Scientific, Technological and Innovation Advances in Botany. Chapter 7, p. 78-104. Atena, Paraná. http://doi.org/10.22533/at.ed.8512014027
18. Silva MC (2018) Essential oils: Characterization, applications and extraction method. Course Conclusion Paper (Bachelor's Degree in Chemical Engineering) - Centro Universitário de Formiga, Minas Gerais.
19. Silva NP (2021) Antimicrobial activity in essential oils and their applications in the food industry. Final Course Work (Bachelor's Degree in Pharmacy) - Federal University of São Paulo, Diadema.
20. Simões CMO, Schenkel EP, Gosmann G, Mello JCP, Mentz LA, Petrovick PR (2004) Pharmacognosy: from plant to medicine (5ed). Florianópolis: UFRGS/UFSC.
21. Slessor KE, Stok JE, Cavaignac SM, Hawkes DB, Ghasemi Y, De Voss JJ (2010) Cineole biodegradation: Molecular cloning, expression and characterisation of (1R)-6b-hydroxycineole dehydrogenase from Citrobacter braakii. Bioorganic chemistry. https://doi.org/10.1016/j.bioorg.2009.12.003
22. Souza SF (2017) Simulation and sensitivity analysis of a reactive distillation column for biodiesel production. Course Conclusion Paper (Technologist in Sugar and Alcohol Production) - Federal University of Paraíba, João Pessoa.
23. Turek C, Stintzing FC (2013) Stability of Essential Oils: A Review. Comprehensive Reviews in Food Science and Food Safety. https://doi.org/10.1111/1541-4337.12006

Figures

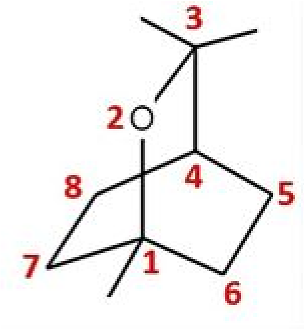

Figure 1

Molecular structure of 1,8-cineole

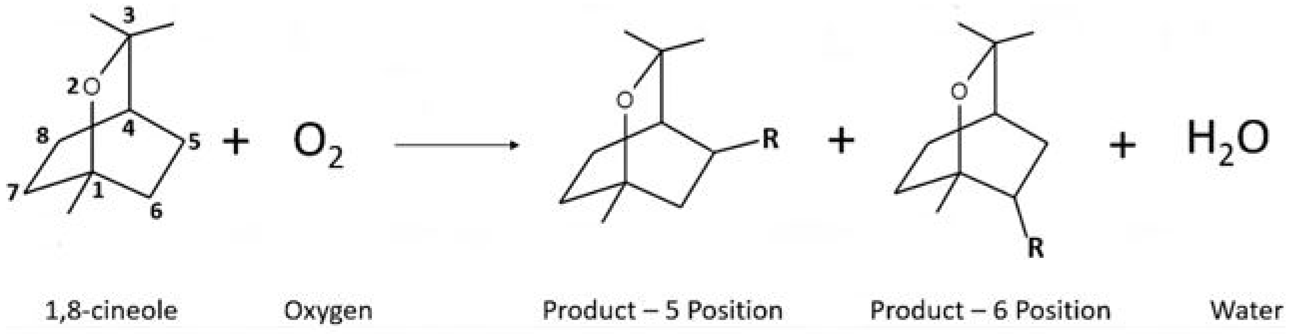

Figure 2

General oxidation reaction of 1,8-cineole

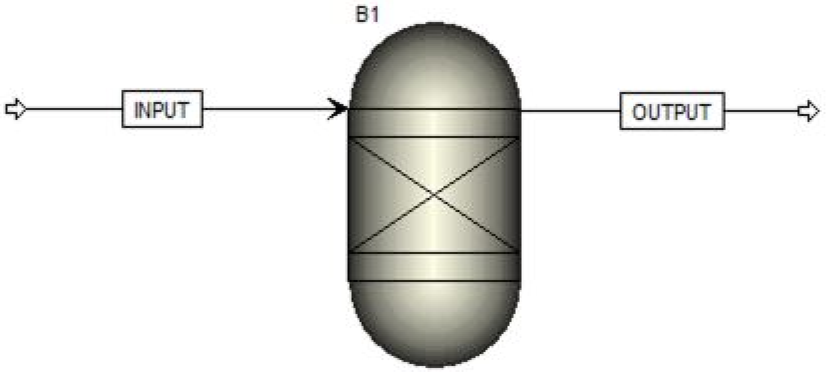

Figure 3

Simulation representation of the degradation process by mild and vigorous oxidation of 1,8-cineole.

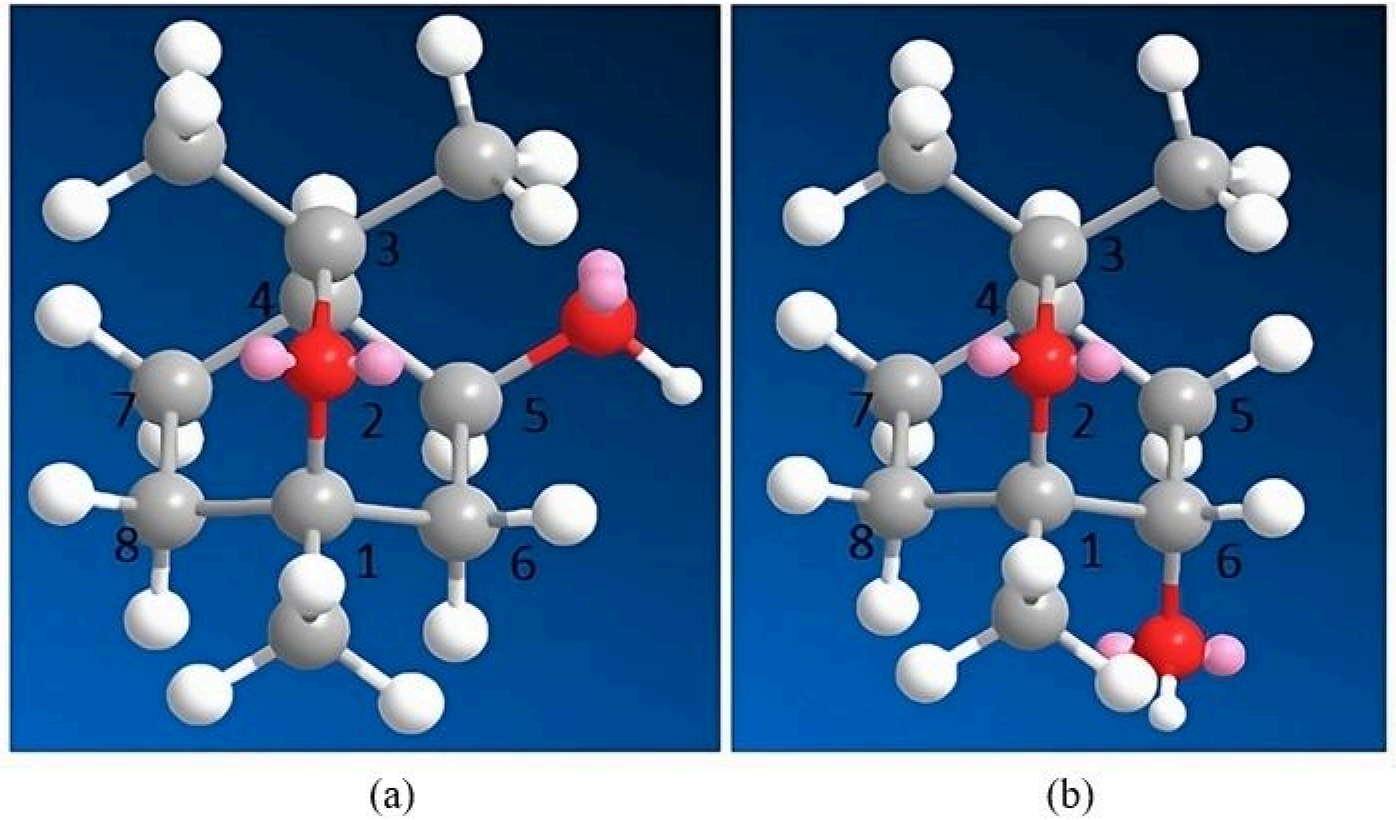

Figure 4

Three-dimensional representation of the alcohol 2 (a) and alcohol 3 (b) molecules

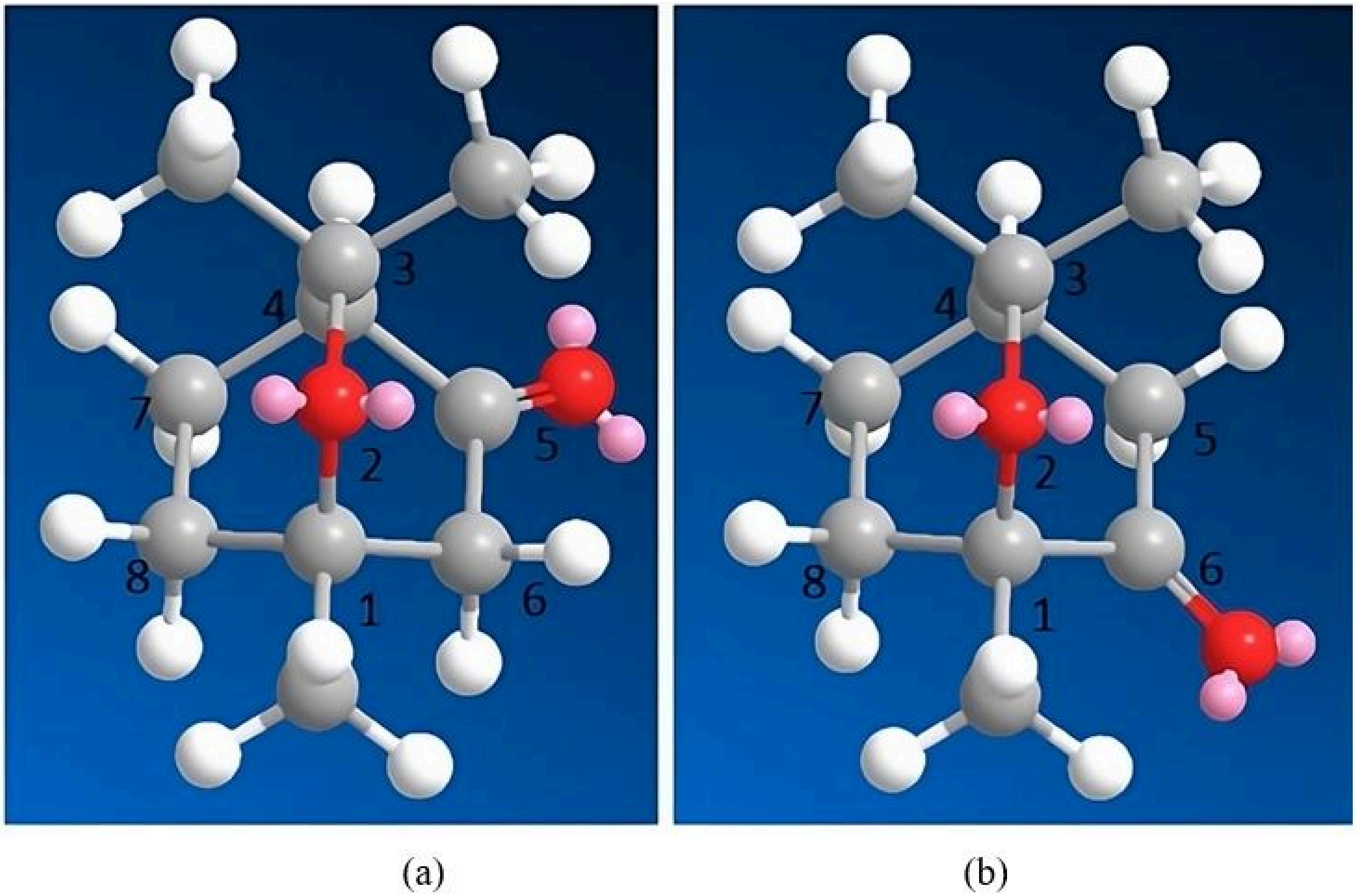

Figure 5

Three-dimensional representation of the ketone 4 (a) and ketone 5 (b) molecules.

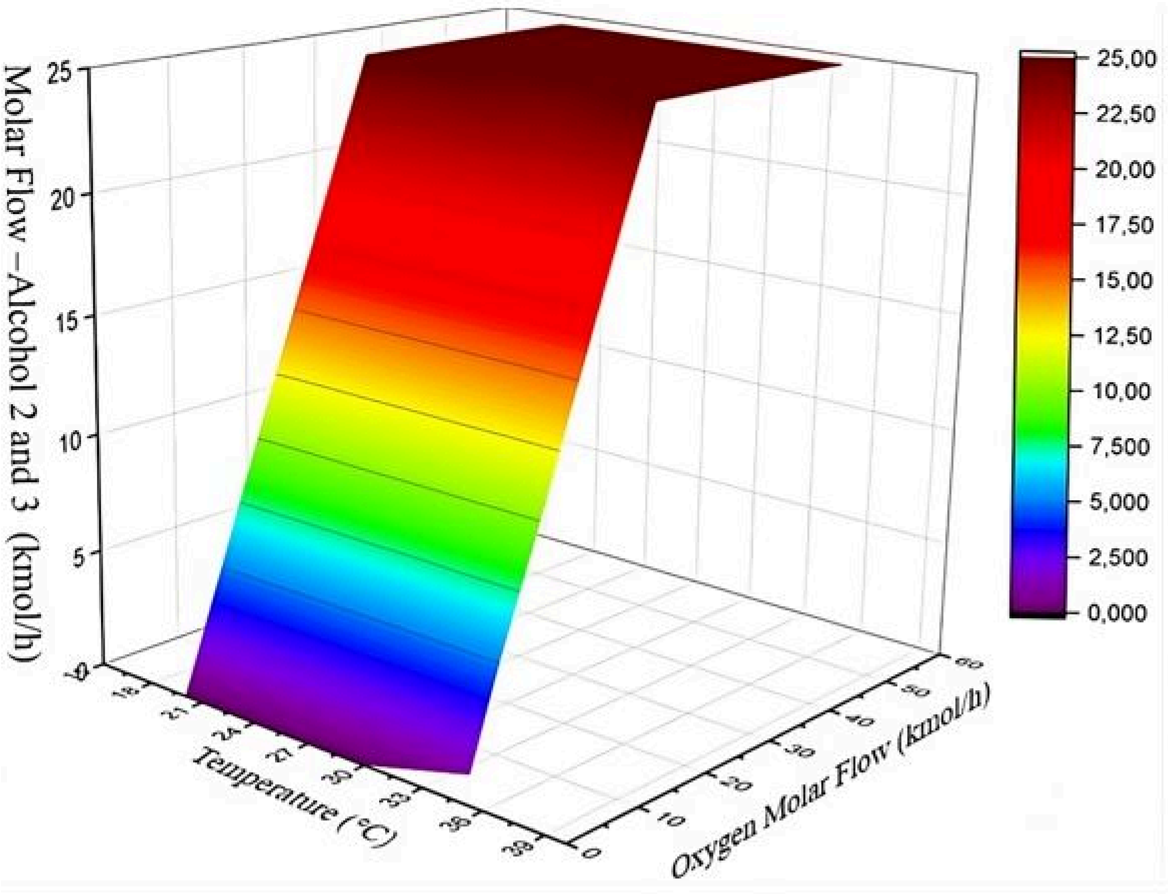

Figure 6

Sensitivity analysis of the 1,8-cineole oxidation to form alcohols 2 and 3, varying the temperature and oxygen flow rate.

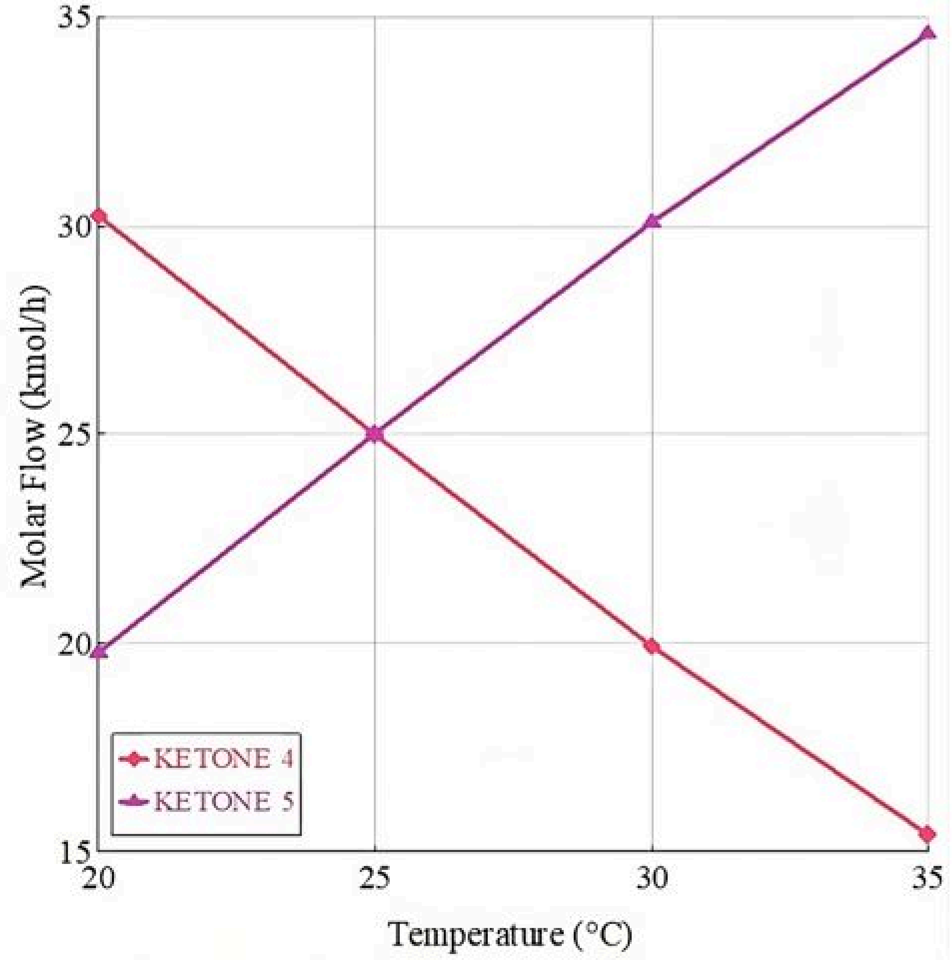

Figure 7

Graphical result of the sensitivity analysis in relation to temperature for the simulation of 1,8-cineole oxidation with the formation of ketones 4 and 5.

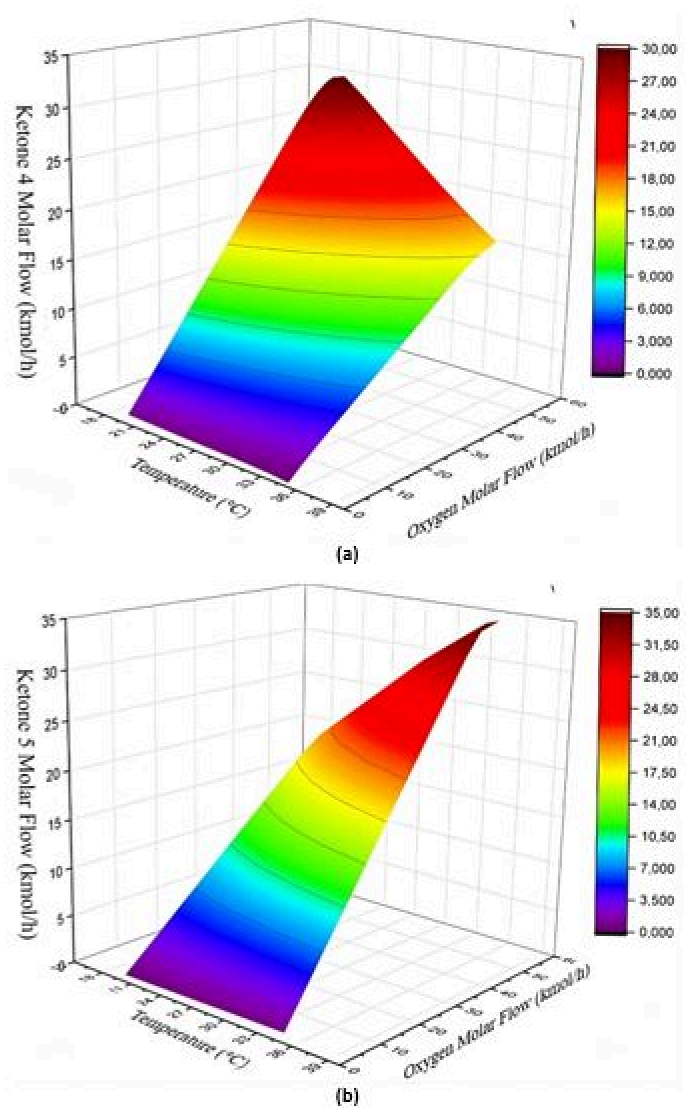

Figure 8

Sensitivity analysis of the 1,8-cineole oxidation simulation for the formation of ketone 4 (a) and ketone 5 (b), varying the temperature and molar oxygen flow rate.

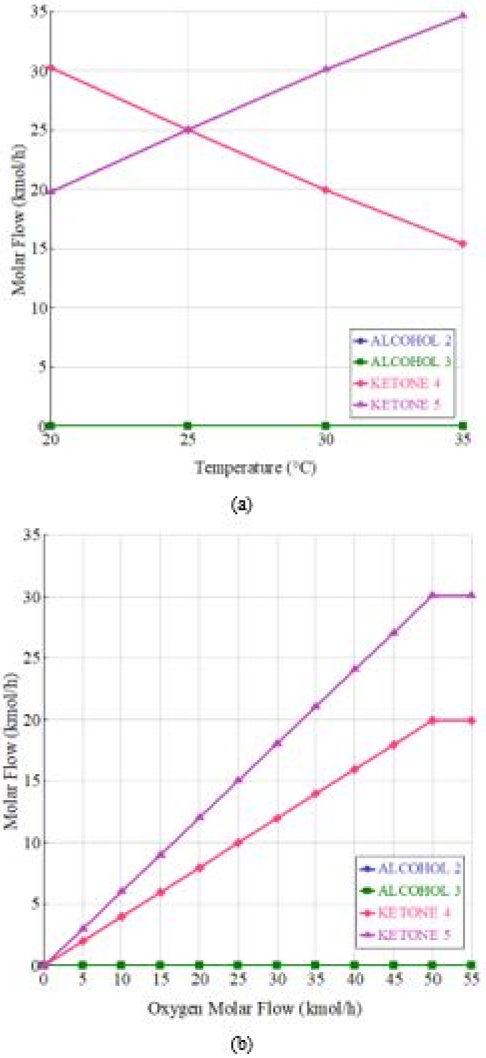

Figure 9

Results of the sensitivity analysis for alcohols and ketones varying the temperature (a) and molar oxygen flow rate (b).