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A Theoretical Study On The Chemical Activities Of The Mainly Oregano Essential Oils

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Abstract: The natural active compounds in Oregano essential oils are extremely beneficial for human health and when used as a drug for treatment. In this study, we have examined the two main Oregano essential oils Thymol and Carvacrol. These oils have many functions; predominantly, in biochemical reactions in metabolism. In our research, we theoretically investigated the chemical activities of Carvacrol and Thymol by using B3LYP/6-31G(d,p) method in the gas, water, and blood phases. The point at which ethanol was used as a solvent was important to the study outcome; hence, in this study; the researchers determined the effective rate of Carvacrol with ethanol to explain the interaction mechanism.

Keywords: *Oregano, Carvacrol, Thymol, Ethanol, Density functional theory (DFT)*

1. Introduction

Ethanol a well-researched substance that is frequently used in medicine across the globe.Ethanol is present in our digestive system, where up to 3 g is fermented each day exclusively as the metabolic fragmentation. Ethanol is not only necessary but also almost all living organisms. Amino acids present in enzymes are used to oxidize ethanol to protect to single cell bacteria [1,2]

The digestion of ethyl alcohol is based on its concentration portal blood. In the liver, a great deal of alcohol is metabolized by ADH or CYP2E1 while a small amount is metabolized in other ways, such as through catalase and exhalation by the lungs. ADH (Alcohol dehydrogenase) is generally saturated and operates at maximal speed, which is nearly 0.1 g/kg/h for males and females, respectively [3]. Ethyl alcohol affects both the function of the liver and the metabolism of gastric alcohol. Alcohol dehydrogenase has a higher activity in males than females, meaning that females indicate a higher exposure to ethyl alcohol than males after intaking of the same amount [4].

ADH contains 2 subunits, each of them composed of 374 amino acids and including zinc in the active center of it. Because of the different types of subunits, more than twenty dimers have been defined and their enzymatic activities are quite different from the others. There are five ADH subtypes (I-V). Type I has the highest activity the ethanol metabolism [5].

CYP2E1 with ADH is the most important enzyme for ethanol metabolism. ADH, like its counterpart CYP2E1, can be stimulated by ethanol [6]. ADH produces acetaldehyde, which is a toxic substance for the liver. Acetaldehyde is reduced by the mitochondrial enzyme acetaldehyde dehydrogenase (ALDH) [4]. For ADH, several subtypes (ALDH 1-9) have been defined. ALDH2 is the most significant subtype related to the ethanol metabolism.

Thyme is an essential oil extract from a plant which, due to its antimicrobial properties, is one of the most widely used and well-known plant extracts. Like Thyme, the Oregano essential oils, carvacrol and thymol, both contain a phenolic

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structure. Due to the functional hydroxyl groups, the antimicrobial properties of these compounds exhibit high redox potentials [7]. In addition to its savory flavor, Carvacrol provides the passage of protons in extracellular fluids hence, when pathogenic microorganisms die, this leads to the shredding of cytoplasmic membranes. Thymol contained in thyme 150 g / mol (C10H14O) has a molecular weight, a white crystal color, a bitter taste acrid, antimicrobial, antioxidant, and antiseptic properties when used as an essential oil [8]. When obtained from thyme, carvacrol and thymol are commonly used in the food and pharmaceutical industries as one of the important essential oils owing to its antimicrobial, anticancer, and antioxidant [9]. When obtained from sunflowers, thymol and carvacrol have been found to inhibit the lipid system. Carvacrol has a more antioxidant effect than thymol [10].

Researchers have studied that Carvacrol and Thymol in vivo systems (such as guinea pigs, rats, mice, etc.); specifically, in terms of biotransformation and metabolization. As a result of this study, the formation of hydroxyl and carboxylic acid-derived metabolites is indicated by means of various analytical techniques [11].

In studies focusing on the liver cirrhosis in rats caused by an ischemia-reperfusion event, Serum AST, ALT, and ALP levels were increased. Carvacrol derived from Thyme was found to maintain the enzyme levels at the desired level owing to the oil's protective effect [12].

Ethanol is first absorbed in the duodenum and a smaller rate in the stomach through diffusion. After ingestion through the mouth, it can be excreted by breath, sweat, orurine. Because of this, it is considered a minor polar substance [13,14]. The absorption rate differences fluctuate in accordance with the genetic and environmental situation as the type of consumption of food and nutrients [15-17]. Also, gender is other significant factor for ethanol metabolism [18,19].

ADH, ALDH, CYP2E1, and catalase are major enzymes for ethanol methabolization[20]. The genes ADH and ALDH, as well as their isoenzymes the ADH1B and ALDH2 genes show different effects for different individuals [21-23].

After intaking of ethanol, it quickly reaches the body fluids in the range of 0.65-0.71 L/kg. Since the quantity of bodily fluids is less in elderly people and in females as compared to middle-aged males, elderly people and females have higher plasma concentrations after ingesting an equal amount of alcohol than middle-aged males. Furthermore, genetic factors such as age, body mass, liver size, and food intake affect the metabolization of ethyl alcohol in the human body [24,25].

ADH1B*3 has a higher ethyl alcohol rate than ADH1B*1 polymorphism [26]. The frequency of ADH1B*2, ADH1B*3, and ALDH2*2 indicate a decreased diagnosed alcohol dependence in East Asian people [27]. ADH1B*3 allele is related to alcohol dependence in Native Americans [28].

In the present study, the interaction between ethanol and carvacrol was studied, as well as thymol in blood. The researchers investigated the interaction of carvacrol and thymol using DFT. Taking the rate of ethanol into account, the interaction energies were calculated between both molecules, thus demonstrating how ethanol interacts with carvacrol and thymol. The electronic differences in the case of the interaction between the hydroxyl group of ethanol with carvacrol and thymol were searched to reveal a probable mechanism to this interaction. The changes in energy were studied to understand the rate of ethanol for carvacrol in the gas phase. It was found that there is a significant interaction between ethanol and carvacrol according to the ethanol rates.

2. Experimental

The researchers studied the chemical activities of the Oregano essential oils Thymol and Carvacrol in different phases (gas, water, blood) and also Carvacrol with ethanol using DFT. A pure DFT method containing Becke's gradient correction for 6-31G (d,p) was used for correlation. B3LYP methods were used for geometry optimization. The correction was carried out by means of the 6-31+g(d,p) functional. These methods and fully optimized geometric structure of the compounds using Gaussian09 were determined and evaluated [29].

3. Results and discussion

The values of carvacrol and thymol in gas, water, blood are given in Table1 and Table 2. We have discussed ethanol interactions with carvacrol, since it was emphasized that antioxidant activity of it was more than thymol in previous studies [10].

Table 1. Carvacrol's values by using DFT (The values are given as Hartree 1Hartree:=627.5095 kcal. mol^{-1}).

	Carvacrol(gas)	**Carvacrol(water)**	**Carvacrol(blood)**
E_0	-464.752464	-464.778078	-464.784152
EZPE	0.216968	0.214162	0.214611
Etot	0.228540	0.224102	0.226167
Hcorr	0.229484	0.225046	0.227111
Gcorr	0.179847	0.178908	0.177601
E0 + EZPE	-464.535496	-464.563916	-464.569541
E0 + Etot	-464.523924	-464.553976	-464.557985
E0 + Hcorr	-464.522980	-464.553032	-464.557041
E0 + Gcorr	-464.572617	-464.599170	-464.606551

Table 2. Ethanol's values (The values are given as Hartree 1Hartree:=627.5095 kcal. mol^{-1}).

	Ethanol(gas)	**Ethanol(water)**	**Ethanol(blood)**
E0	-155.046213	- 155.066269	-155.068763
EZPE	0.080161	0.078421	0.078760
Etot	0.084443	0.082114	0.083142
Hcorr	0.085387	0.083058	0.084086
Gcorr	0.054782	0.053466	0.053251
E0 + EZPE	-154.966052	-154.987849	-154.990003
E0 + Etot	-154.961770	-154.984156	-154.985621
E0 + Hcorr	-154.960826	-154.983212	-154.984677
E0 + Gcorr	-154.991431	-155.012804	-155.015511

The free energy values of Ethanol-Carvacrol rates in the gas phase are given in Table3.

Table 3. The free energy values of the Ethanol-Carvacrol rates in the gas phase

DFT (GAS)(Separately)	**ΔG Hartree**	**DFT (GAS)(Together)**	**ΔG(Difference) Hartree**	**ΔG Hartree**	**ΔG(Difference) kcal/mol**
1Ethanol + 1Carvacrol	-619.564050	**1Ethanol- 1Carvacroll**	-619.561428	0.002620	1.644075
2Ethanol + 1Carvacrol	-774.555480	**2Ethanol- 1Carvacrol**	-774.543414	0.012070	7.574040
3Ethanol + 1Carvacrol	-929.546910	**3Ethanol- 1Carvacrol**	-929.526238	0.020670	12.970621
4Ethanol + 1Carvacrol	-1084.538340	**4Ethanol - 1Carvacroll**	-1084.515118	0.023220	14.572026
5Ethanol + 1Carvacrol	-1239.529770	**5Ethanol - 1Carvacrol**	-1239.492181	0.027590	17.312360
1Carvacrol + 1Ethanol	-619.564050	**1Carvacrol -1Ethanol**	-619.561439	0.002610	1.637799
2Carvacrol + 1Ethanol	-1084.136700	**2Carvacrol -1Ethanol**	-1084.117317	0.019400	12.173684
3Carvacrol + 1Ethanol	-1548.709300	**3Carvacrol3-Ethanol**	-1548.681263	0.028000	17.570266
4Carvacrol + 1Ethanol	-2013.281900	**4Carvacrol - 1Ethanol**	-2013.252508	0.029390	18.443760
5Carvacrol + 1Ethanol	-2477.85452	**5Carvacrol - 1Ethanol**	-2477.815320	0.039200	24.598372

Table 4. The interaction of carvacrol and thymol with Ethanol's values by Using DFT (The values are given as Hartree and 1Hartree:=627.5095 kcal. mol^{-1}).

Compound	**ΔG(Hartree)**	**ΔG(kcal/mol)**
Carvacrol-the methyl group of ethanol	-608.170047	-381632.482108
Carvacrol-the hydroxyl group of ethanol	-603.073791	-378434.533054
Thymol-the methyl group of ethanol	-608.171563	-381633.433412
Thymol-the hydroxyl group of ethanol	-608.179122	-381638.176757

The interactions between the two molecules were shown to change the charge transference and structural modification formed a function of the total energy values. All these factors are associated with different reaction schemes. For the present problem, different ratios for carvacrol and ethanol were studied using the B3LYP/6-31G(d,P) method to analyze the different phases of the reaction. Carvacrol was found to be able to completely eliminate alcoholic liver damage when the dosage of the active ingredient was adjusted [30]. The interaction of carvacrol and thymol with Ethanol's values are given in Table 4. The interaction of Carvacrol with Ethanol is given given in Figure 1.

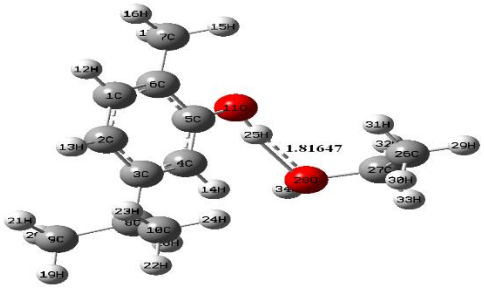

Figure 1. The interaction of Carvacrol with Ethanol

There is a hydrogen bond formation between Carvacrol with Ethanol as shown in Figure 1.

Firstly, there is an interaction with the methyl group (CH_3), and the second the interaction with the hydroxyl (OH) fragment. The interaction energy was calculated between both molecules and given in Table 4. Firstly, the energy value for the interaction the methyl group of ethanol with carvacrol is -381632.482108 kcal/mol and hydroxyl fragment of ethanol with carvacrol is -378434.533054 kcal/mol. When we looked for thymol for the first one these values are -381633.433412 and -381638.176757. The interaction methyl group fragment of ethanol is higher but for thymol hydroxyl fragment of ethanol is higher than the others. Because of the position of OH functional group of thymol and carvacrol [7].

The free energy values in Table 3: 1.6440749 kcal/mol, 7.5740397 kcal/mol, 12.970621 kcal/mol, 1.6377998 kcal/mol,12.173684 kcal/mol,17.570266 kcal/mol. When we looked the free energy values for Carvacrol-Ethanol separately and together:

We change the rate of Ethanol;

7.5740397-1.6440749=5.929965
2) 12.970621-7.5740397= 5.396581
When we change the ratio of carvacrol**;**
12.173684-1.6377998= 10.53588
2) 17.570266-12.173684= 5.396582

2-Carvacrol-1Ethanol (together) and 2-Carvacrol-1-Ethanol (separately) the free energy values are higher than the other. When we looked at the calculations; 1Ethanol-2Carvacrol, the value of 10.53588 is maximum effective point.

4. Conclusion

As a result of comparing the chemical activities of Oregano essential oils, Thymol and Carvacrol in different phases (gas, water, blood) and also Carvacrol with ethanol; Thymol has more chemical activities than carvacrol. Therefore these two substances can be used as antioxidant agent and Thymol's energy value is higher than carvacrol. As a result of this; the rate of Carvacrol with Ethanol; the maximum efficient point was 1 Ethanol: 2 Carvacrol.

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