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The Synthesis and Spectral Analysis of Au(III) Complex of Caffeine and Nicotinamide

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Abstract: In the present study, an Au(III) complex of caffeine (CA) and nicotinamide (NA) was synthesized under reflux conditions. The structural characterization of the complex was investigated by using physico-chemical, spectral methods (UV/Vis, LC-MS, FT-IR, ^{1}H and ^{13}C NMR, XRD) and thermal analysis. The spectroscopic results of mixed ligand complex of CA and NA with the Au(III) suggested that N_9 and N_1 atoms of the ligands are coordinated to gold ion. Based on spectral and magnetic moment measurements, the complex was identified as in square-planar structure. From these analyses, it is predicted that the complex has the form of $[Au(CA)_2(NA)_2]Cl_3.2H_2O$.

Keywords: Caffeine, nicotinamide, Au(III), synthesis, spectroscopy.

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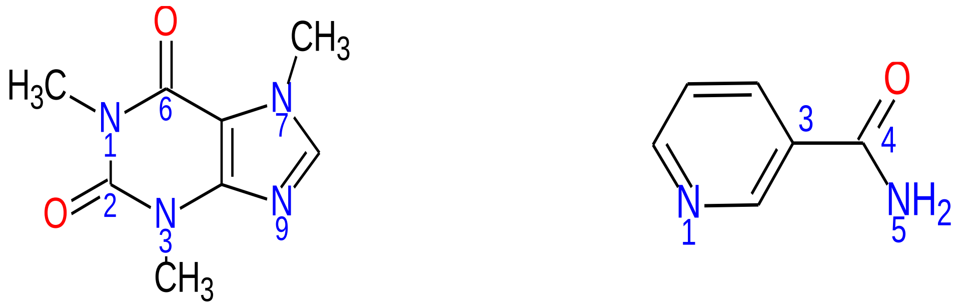
INTRODUCTION

The purine alkoloid caffeine (CA), 1,3,7-trimethylxanthine, is an important component of many popular drinks, especially coffee and tea, but most chemists know little about its molecular and biochemistry (1). Caffeine is well known as a antimalarial agent and has the ability to solubilize a wide variety of therapeutic drugs. While there are many reports about its anticancer and antioxidant properties, there is also a strong belief that consumption in high amounts of caffeine carries a higher risk of osteoid problems developing, including osteoporosis, as well as problems with metal absorption, excretion and readsorption processes in intestines and kidneys (2).

Nicotinamide (NA) is a component of both co-enzyme of nicotinamide adenine dinucleotide (NAD) and vitamin B complex (3). These are very important to transfer hydrogen in cell respiration. The presence of the pyridine ring in which are adducts of nicotinamide numerous naturally abundant compounds is also of scientific interest. Therefore, the structure of nicotinamide has been the subject of many studies (4, 5).

The chemical structures of nicotinamide and caffeine are shown below**.** Structurally, caffeine contains two aromatic rings that affect the solubility of the aromatic hydrotropic agent (6-8). In Scheme 1, caffeine has a methyl group at the N_7 site, which blocks the interaction of metal cations with the N_7 atom. N_1 and N_3 are also blocked by the methyl group. Thus, in caffeine N_9 atom is the target of metal cation interaction, while the major binding site in nicotinamide is the N_1 atom (9).



Caffeine

Nicotinamide

Scheme 1: The structures of caffeine and nicotinamide.

In the present study, the preparation and structural elucidation of the Au(III) complex of mixed ligand CA and NA is undertaken by using different methods such as physico-chemical, spectroscopic methods (UV/Vis, Mass (LC-MS), FT-IR, ^{1}H NMR, ^{13}C NMR and XRD) and thermal analysis.

EXPERIMENTAL

Materials and measurements

All reagents were purchased from commercial sources and used as supplied. The magnetic moment results were obtained from MK-1 Sherwood scientific magnetic susceptibility balance. Conductivity measurements were determined in DMSO using an Inolab Thermal 740P. Elemental analyses for C, H and N were recorded with a Costech elemental analyzer. UV/Vis spectra were performed with a Shimadzu UV-1700 Pharma spectrophotometer in the 200-800 nm range. For the mass (LC-MS) spectra, we used an AB-SCIEX Triple TOF 4600 System. FT-IR spectra were measured with a Shimadzu IR-470 spectrometer as KBr pellets in the frequency range 400-4000 cm^{-1}. ^1H NMR and ^{13}C NMR spectra were obtained in DMSO on a Bruker, DPX-400 spectrometer. Shimadzu XRD-6000 was employed for the XRD analyses. The curves of thermal analyses (TG and DTA) were observed on a Seiko Exstar TG/DTA 6200 thermal analyzer in a flowing air atmosphere with a heating rate of 10 °C min^{-1} using a sample size of 5-10 mg and platinum crucibles.

Synthesis of Au(III) complex

Caffeine (CA) of 0.388 g ($2x10^{-3}$ mol) was dissolved in water. An aqueous solution of the metal salt was added and placed in a magnetically-stirred 25 mL round-bottomed flask. This was followed by the addition of an ethanolic solution (0.244 g, $2x10^{-3}$ mol) of nicotinamide (NA) at the molar ratio of 1:2:2 (M:CA:NA). The system was refluxed for five hours at 75-80 °C. The yellow solid material obtained was washed in water, recrystallized with ethanol:water mixture, and dried. The yields were obtained at 88%. All complexes were air-stable and soluble only in organic solvents.

$[Au(CA)_2(NA)_2]Cl_3.2H_2O$: Yield (%): 88. Color: Yellow. M.P. (°C): 205. Elemental Analysis (%): Calcd.: C 34.67, H 3.72, N 17.33, O 13.21, Cl 10.99, Au 20.08; Found: C 34.46, H 3.64, N 17.29, O 13.17, Cl 10.94, Au 20.00. FT-IR (cm^{-1}): 3347.08 ν(NH), 1692.22 ν(C=O), 1603.76 ν(C=N), 1499.92 ν(C=C), 1221.67 ν(C-N), 597.27 ν(M-N). UV-Vis. (nm): 511, 242. Magnetic Moment (BM): Diamagnetic. Conductivity ($\Omega^{-1}cm^2mol^{-1}$): 88.00. MS (m/z, EI): 968.97; Found: 969.30.

RESULTS AND DISCUSSION

Elemental analysis C, H, N, O and metal determination are in good agreement with the general formula given for the complex. The molar conductance value found for this complex at the concentration of 10^{-3} mol/L is 86 $ohm^{-1}mol^{-1}cm^2$. The value for electrolyte in DMSO is of the order of 65-90 $ohm^{-1}mol^{-1}cm^2$. Hence, this complex can be regarded as an electrolyte (10). The magnetic moment of the Au(III) complex was 0.00 BM, indicating that the Au(III) complex is typically a low-spin complex with square-planar structure. The value of μ_{eff} for Au^{3+} complex is diamagnetic. The absorption bands determined in the electronic spectra of the Au(III) complex also support a square-planar structure (11). From the magnetic and conductometric analysis, it is predicted that the complex is in the form of $[Au(CA)_2(NA)_2].2H_2O$. The obtained complex is solid, insoluble in water, but soluble in DMSO, DMF, THF.

The mass (LC-MS) spectrum of Au(III) complex is given in Figure 1.

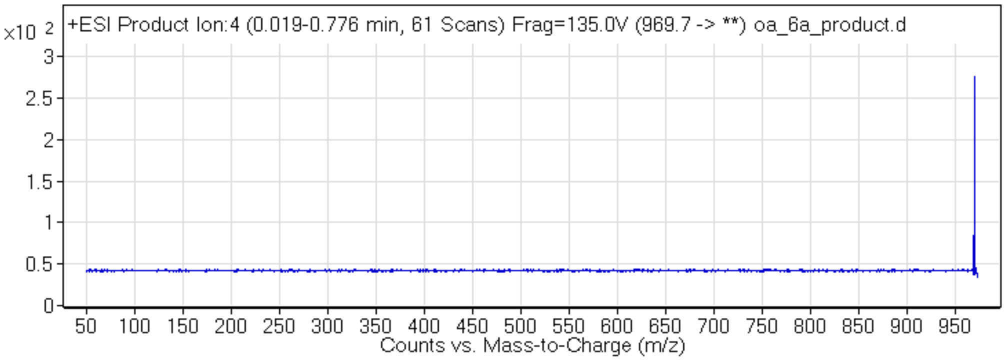


Figure 1: Mass (LC-MS) spectrum of $[Au(NA)_2(CA)_2].2H_2O]$

In Figure 1, there is one peak and this is in agreement with the molecular weight of the complex. This result shows that it is a complexation.

UV-Visible spectra

The UV-Visible spectra of the ligands and Au(III) complex in DMSO showed absorption bands between 290-850 nm (Table 1).

Table 1. UV-Visible spectra of the free ligands and Au(III) complex.

Compound	λ $_{max}$(nm)	ABS	Assignment
NA	260	1.052	π-π*
	340	0.553	n-π*
CA	275	1.774	π-π*
	316	0.006	n-π*
	365	0.014	n-π*
Au(III) complex	242	2.552	π→π* and n→π* $^1A_{1g}$ (D) → ^1E_u (D)
	511	0.888	$^1A_{1g}$ (D) → $^1A_{2g}$ (D)

In the UV-Visible spectra of NA, CA and Au(III) complex, the presence of a wide range of bands are due to both n-π* and π-π* and due to a charge transfer transition arising from π electron interactions between the metal and ligand that involves either a metal-to-ligand or ligand-to-metal electron transfer.

The absorption spectra of the Au(III) complex demonstrates an absorption band at 242 nm, which is attributed to the electronic transition of $^1A_{1g}$ (D) → ^1E_u (D), while the band at 511 nm is caused by the electronic transition of $^1A_{1g}$ (D) → $^1A_{2g}$ (D). These transitions and assignments indicate that the Au(III) complex has square-planar geometry (12, 13).

FT-IR spectra

The FT-IR spectra of the CA and NA and gold complex are given in Figure 2.

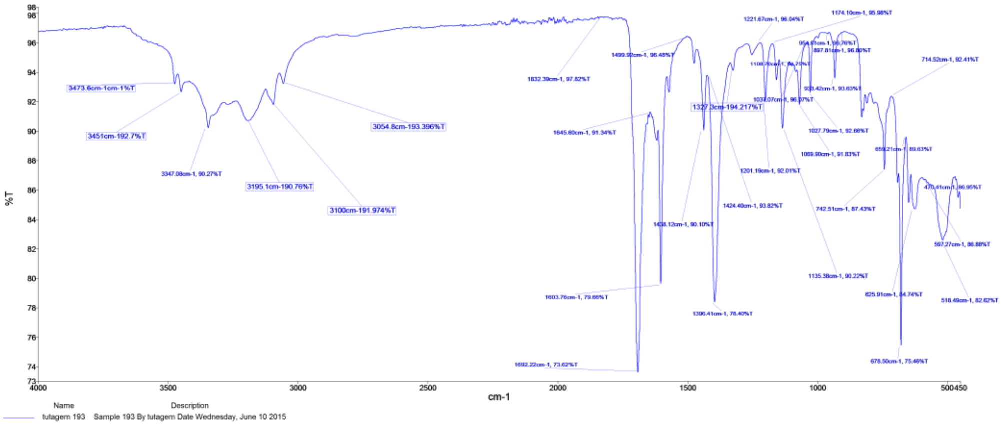


Figure 2: FT-IR spectrum of $[Au(NA)_2(CA)_2].2H_2O]$.

The FT-IR spectrum of CA demonstrates strong bands at 1720 and 1658 cm^{-1} that may be attributed to the $\nu_{(C=O)}$ and $\nu_{(C=N)}$ stretching frequencies, respectively (14, 15). These bands are shifted to lower frequencies in the complex by 1692 cm^{-1} and 1603 cm^{-1}, respectively. These results indicate that the coordination of CA to the metal ions is through the nitrogen atom N_9 (16).

In the FT-IR spectrum of NA (14, 15), the band at 1680 cm^{-1} which is assignable to nicotinamide band arising mainly from the $\nu_{(C=O)}$ stretching vibration in free NA, which is also found at the frequency range 1692 cm^{-1} in the Au(III) complex. The bands at 1612cm^{-1} and 1255 cm^{-1} are due to $\nu_{(C=N)}$ and $\nu_{(C\text{-}N)}$ stretching vibrations and they move to lower wavenumbers (1603 cm^{-1} and 1221 cm^{-1}) compared to free NA. The coordination through the nitrogen atom in $\nu_{(C=N)}$ and $\nu_{(C\text{-}N)}$ groups is further supported by the occurrence of a new band at 597 cm^{-1} in the spectra of the complex which may be assigned to $\nu_{(M\text{-}N)}$ (17). The free NA shows a medium intensity band at 3210 cm^{-1} assigned to $\nu_{(NH)}$ vibrations, which has been observed in the 3347 cm^{-1} region for the complex. It can be observed that there is no considerable shift in the $\nu_{(NH)}$ vibrations in the case of the complex, compared to nicotinamide, indicating non-involvement of the amide NH function in coordination.

^{1}H and ^{13}C spectra

^{1}H and ^{13}C NMR data of the NA, CA and Au(III) complex are given Figure 3 and 4.

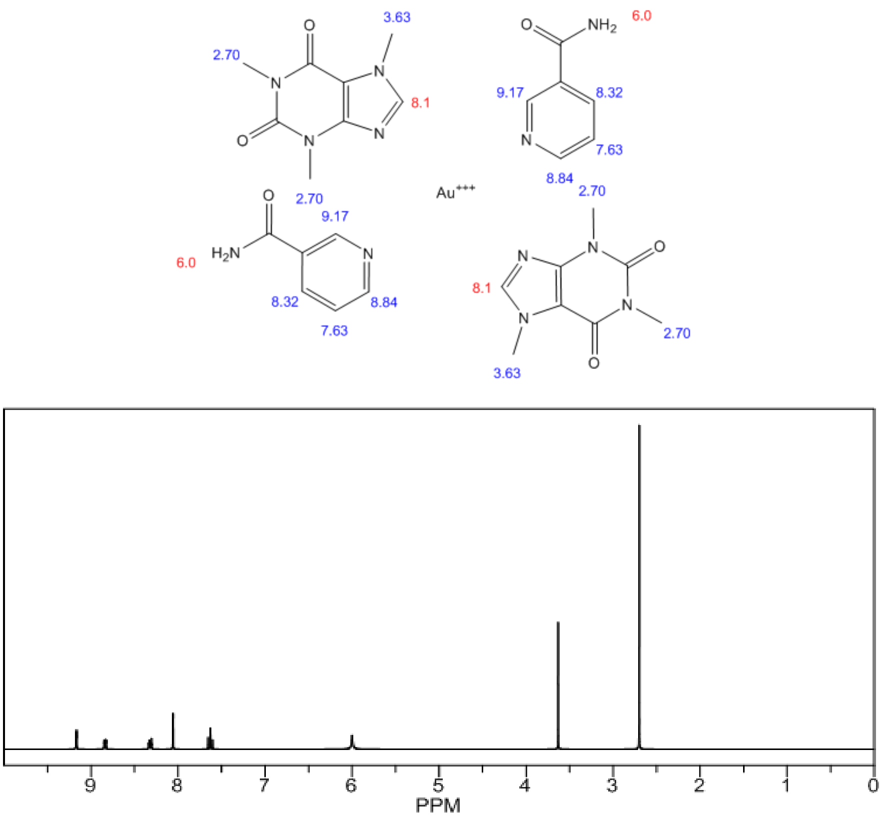


Figure 3: ^{1}H NMR spectrum of [Au(NA)$_2$(CA)$_2$].2H$_2$O]

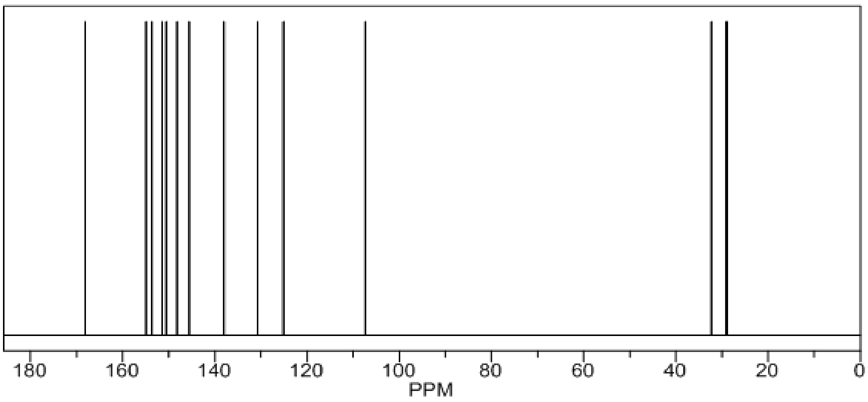


Figure 4: ^{13}C NMR spectrum of [Au(NA)$_2$(CA)$_2$].2H$_2$O]

The ^{1}H NMR spectra of caffeine in d-DMSO has proton signals at δ: 2.70 (s, 3H, N_1- CH_3), 2.70 (s, 3H, N_3-CH_3), 3.63 (s, 3H, N_7-CH_3) and 8.10 ppm (s, 1H, C_8-H), while nicotinamide has signals at δ: 9.17 (d, 1H, C_2-H), 8.32 (d, 1H, C_4-H), 7.63 (m, 1H, C_5-H), 8.84 (d, 1H, C_6-H), and 6 ppm (s, 2H, NH_2).

The ^{13}C NMR spectrum of caffeine shows signals at δ: 27.9 (s, N_1-CH_3), 29.7 (s, N_1-CH_3), 33.5 (s, N_7-CH_3), 152 (s, C_2), 149 (s, C_4), 108 (s, C_5), 155 (s, C_6) and 141 ppm (s, C_8), while nicotinamide-caffeine has them at δ: 144 (s, C_2), 139 (s, C_3), 127 (s, C_4), 132 (s, C_5), 149 (s, C_6) and 170 ppm (s, C_7). According to the ^{1}H and ^{13}C NMR data, little shifting is determined in the obtained complexes. These signals support the idea that nicotinamide and caffeine are coordinated with metal ions through N_9 and N_1 (18).

XRD spectra

The XRD (powder pattern) values of the complex were calculated in an X-Ray diffractometer and the unit cell parameters were recorded from 2θ values with the help of a computer. Powder XRD patterns of complex consist of seven important peaks in the range 5-50° (2θ). The interplanar spacing (d) was calculated from the positions of intense peaks using Bragg's relationship. XRD data is given in Figure 5.

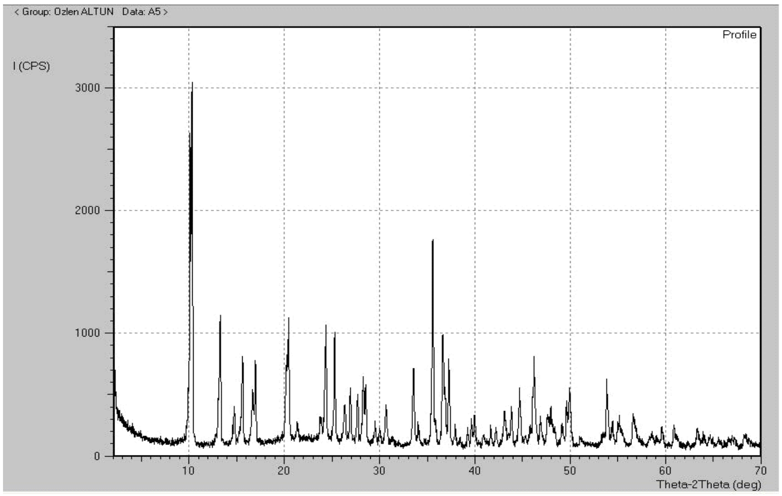


Figure 5: XRD spectrum of $[Au(NA)_2(CA)_2].2H_2O]$.

According to Figure 5, the 2θ values with maximum intensity of the peaks for Au(III) complex are observed to be 10.2011, 13.2255, 24.3123, 25.2565, 26.9073, 35.8669 and 37.2506 (2θ) which corresponds to d: 8.66442, 6.68906, 3.65805, 3.52339, 3.31086, 2.50169 and 2.4118, respectively. All the peaks calculated on the obtained values of interplanar distance are compared with the recorded ones. This implies that Au(III) complex has square-planar geometry in structure.

Thermal Analysis

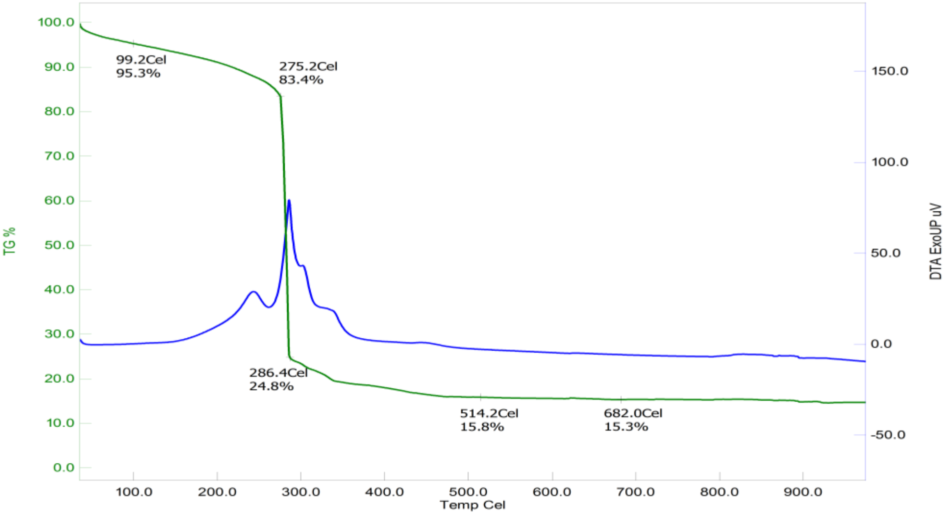


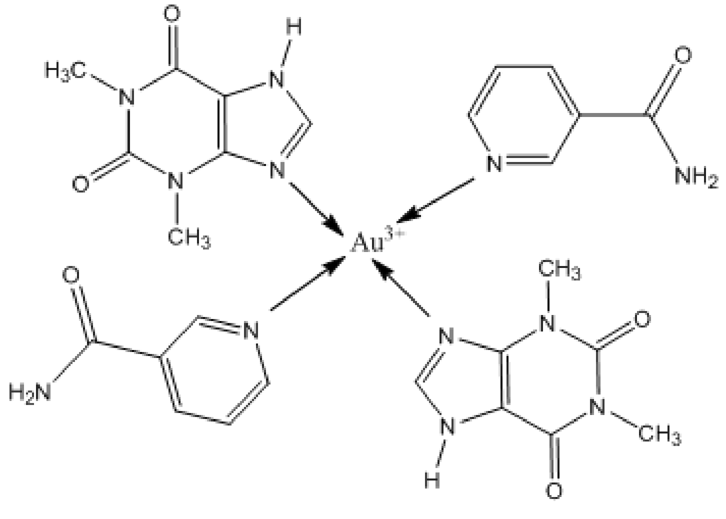
Figure 6: TG-DTA spectrum of $[Au(NA)_2(CA)_2].2H_2O]$

TG-DTA analysis was completed in the temperature range of 25 °C and 1200 °C in static atmosphere of dry air to examine thermal stabilities of complexes. Thermal analysis data of the Au(III) complex are summarized in Figure 6.

The thermal behavior of the Au(III) complex is discussed below; the first stage decomposition is endothermic in the range of 25-200°C with a mass loss of 4.7%, which corresponds to the loss of 2 moles of water. The second stage of decomposition is also endothermic in the range 200-500°C, which is the decomposed organic component (83.4%). The remaining compound over 500 °C is determined as Au (15.80%). These results are in good agreement with the suggested structures of the complex. It is confirmed that the complex contains water in the structure. As a result of the thermal study, qualitative conclusions can be made for the stability of the complex.

CONCLUSION

In the present paper, small changes in the spectral analyses were determined for the synthesized Au(III) complex. According to physico-chemical, spectrophotometric, and thermal analysis results, the reaction of a mixed ligand of CA and NA with Au(III) is a complexation reaction. Two molecules of mixed ligand react with one molecule of Au(III) ion. Accordingly, the following is the proposed structure of the mixed ligand complex of caffeine and nicotinamide in the presence of Au(III), the following complexation scheme is obtained:



Scheme 2: Complexation of gold(III) with caffeine and nicotinamide in a (1:2:2) ratio.

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support received did not lead to any conflict of interests regarding the publication of this manuscript. There is no need for Trakya University's confirmation to publish this manuscript.

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