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ОЛЕИНОВАЯ КИСЛОТА КАК ЭФФЕКТИВНОЕ ПОВЕРХНО-АКТИВНОЕ ВЕЩЕСТВО ДЛЯ МИКРОЧАСТИЦ ПОЛИ (МОЛОЧНОЙ КИСЛОТЫ): ИССЛЕДОВАНИЕ DFT

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Целью данного исследования было изучение взаимодействия олеиновой кислоты (OA) с микрочастицами полимолочной кислоты (PLA) в фазах хлороформа и дихлорметана с использованием методов теории функционала плотности (DFT) и теории функционала плотности, зависящей от времени (TDDFT). Исследование проведено на уровне теории B3LYP-D3/6-31+G**. Энергия связи, дипольный момент и термодинамические параметры показывают, что взаимодействие OA и PLA через связи C=O….HO в наиболее устойчивом состоянии (состояние I) в фазе хлороформа сильнее, чем в фазе дихлорметана. Отрицательные значения термодинамических параметров наиболее стабильного комплекса и графиков МЭП показали, что OA оказывает положительное влияние на адсорбционное поведение PLA. Присутствие OA изменило структуру PLA на основании теоретических УФ-Vis и инфракрасных (ИК) спектров. Результаты показали, что использование поверхностно-активного вещества OA может улучшить дисперсию и совместимость с матрицей PLA.

Ключевые слова: олеиновая кислота, поли (молочная) кислота, поверхностно-активное вещество, дисперсия, совместимость

OLEIC ACID AS AN EFFECTIVE SURFACTANT FOR POLY (LACTIC ACID) MICROPARTICLE: A DFT STUDY

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This study aimed to investigate the interaction of oleic acid (OA) with poly (lactic acid) (PLA) microparticle in chloroform and dichloromethane phases using density functional theory (DFT) and time-dependent density functional theory (TDDFT) methods. The study was conducted at the B3LYP-D3/6-31+G** level of theory. The binding energy, dipole moment. and thermodynamic parameters show that the interaction between OA and PLA via C=O….H-O bonds in the most stable state (state I) in the chloroform phase is stronger than in the dichloromethane phase.

Negative values of the thermodynamic parameters in the most stable complex and the MEP graphs showed that OA has a positive impact on the adsorption behavior of the PLA. The presence of OA altered the structure of PLA based on theoretical UV-Vis and Infrared (IR) spectra. The findings revealed that using the OA surfactant can improve dispersion and compatibility with the PLA matrix.

Keywords: oleic acid, poly (lactic acid), surfactant, dispersion, compatibility

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INTRODUCTION

Common polymers are extensive molecules made up of repeating units known as monomers. They are extensively utilized in different industries because of their adaptability and strength. Conversely, cancer growth [1-5] is a multifaceted process that can result from a range of factors including genetic mutations, environmental exposures, and certain polymers. As a result, scientists globally are diligently working towards finding a cure for this disease and other diseases [6-10]. Also, conventional polymers, derived from petrochemical sources, present a significant environmental challenge due to their non-degradability and limited recyclability at the end of their useful life. To address this issue, extensive research has been conducted on biodegradable polymers as a promising solution to promote sustainability and create an eco-friendly environment by replacing the reliance on conventional polymers [11]. Biodegradable polymers are widely utilized in diverse biomedical applications due to their biocompatibility, non-toxicity, and non-immunogenic properties [12]. Poly (glycolic acid) (PGA), poly (lactic acid) (PLA), and poly (lactic-co-glycolic acid) (PLGA) copolymers are synthetic biodegradable polymers that were introduced during the latter half of the 20th century. Subsequently, these materials received approval from the Food and Drug Administration (FDA) and have since become the predominant choice of materials in the field of biomedicine [13]. Over time, their applications have significantly expanded, and they are now widely used to create musculoskeletal tissue engineering scaffolds and other biomedical products [14, 15]. PLA is a readily available, hydrophobic, aliphatic polyester with high transparency [16], elastic modulus, and thermal processability [17], making it ideal for biomedical applications [18, 19]. Introducing this carrier as a novel therapy can be a promising solution to mitigate the harmful side effects caused by anti-inflammatory drugs, while also enhancing the overall effectiveness of the treatment [20].

Broadening the scope of utilization for a biocompatible, non-toxic, and biodegradable bioplastic has been a challenge due to its limitations in areas such as packaging, engineering, medical, and other applications [16]. PLA, a known bioplastic, exhibits slow crystallization, Limited thermal stability, and pronounced brittleness. In order to overcome these limitations, a range of bio-fillers have been incorporated into the PLA matrix to create blend films and improve their characteristics. These fillers comprise of cellulose nanocrystals modified with ammonium salt [21], coffee grounds [22], keratin [23], and fish gelatin [24]. Likewise, elastin has been blended with the PLA matrix and other polymers to fabricate tissue scaffolds containing fibers and extracellular matrix [25]. To achieve a stable dispersion and enhance compatibility between the PLA matrix and surfactants, it is often essential to perform chemical modifications such as grafting and crosslinking of surfactants. These modifications help to ensure that the surfactants are well-integrated into the matrix, leading to improved performance and functionality of the final product.

Oleic acid (OA) is a commonly employed surfactant characterized by its polar functional group -COOH, which is connected to lengthy hydrocarbon chains. Numerous studies have examined the effectiveness of OA as a surfactant. In a particular investigation conducted by Zhang et al., the tribological properties of PAO4 base oil were explored by incorporating an oleic acid surfactant along with tungsten disulfide (WS_2) nanoparticles. They discovered that the presence of OA improves dispersion stability [26]. Today's large computational tools enable designing and optimizing highly effective PLA matrix dispersion, eliminating the need for expensive long-term experiments. This study aimed to investigate the effect of OA as a surfactant on the PLA matrix using density functional theory. This was done to improve the compatibility of the acid with PLA, which has not been extensively studied before using DFT. In a prior investigation, we examined both theoretical and experimental [27] research on the interactions between sulfasalazine and poly (lactic acid). The findings showed that the presence of SSZ led to a modification in the PLA structure. Therefore, to achieve a stable dispersion and enhance compatibility between the PLA microparticle and oleic acid surfactant, their interaction was studied using DFT methods.

COMPUTATIONAL METHOD

Density Functional Theory (DFT) is a computational approach in quantum mechanics applied in the fields of chemistry and physics for studying the electronic structure of molecules and solids [28, 29]. The optimized structure of the PLA microparticle molecule, OA, and, as well as their complexes, were determined employing DFT and TDDFT methodologies at the B3LYP-D3 level of theory [30, 31]. The calculations were performed using Gaussian 09 software [32] with the 6-31+G** basis set. This theoretical level, B3LYP-D3/6-31+G(d,p), is known for its high accuracy in studying various dimer systems involving non-covalent drug-polymer interactions [33, 34]. Following geometry optimization, the binding energy (E_{bin}) was determined as the zero-point corrected energy (ZPE) using the aforementioned theoretical level and the general formula below:

$$E_{bin} = (E_{OA/PLA} + ZPE) - \\ - (E_{PLA} + ZPE) - (E_{OA} + ZPE) \quad (1)$$

Where E_{PLA} and E_{OA} are the total energies of the individual components and $E_{OA/PLA}$ is the total energy of the complex formed. We used the Polarizable Continuum Model (PCM) [35] to account for the solvent effect and evaluated the adsorption system of OA on PLA in both chloroform and dichloromethane phases. The quantum molecular descriptors (QMDs) were utilized to calculate the physicochemical properties of the interacting systems as follow:

$$\mu = -\frac{1}{2}(I + A) \quad (2)$$

$$\chi = -\mu \quad (3)$$

$$\eta = \frac{1}{2}(I - A) \quad (4)$$

$$S = \frac{1}{2\eta} \quad (5)$$

$$\omega = \frac{\mu^2}{2\eta} \quad (6)$$

According to Koopmans' theorem, the ionization potential (I) and electron affinity (A) of a molecule can be calculated by the negative orbital energies of its highest occupied molecular orbital (HOMO) and lowest unoccupied molecular orbital (LUMO), respectively. Other important parameters for describing the electronic structure of a molecule include global softness (S), chemical potential (μ), electronegativity (χ), global hardness (η), and electrophilicity index (ω) [36].

RESULTS AND DISCUSSION

Binding energy and thermodynamic parameters

Initially, the molecular electrostatic potential (MEP) graphs were used to get the best structural configurations for OA interaction with PLA microparticles. The MEP of PLA and OA molecules presents that the negative charges distributed on O atoms (red region) in the PLA and OA molecules, and the positive charges of the molecules are mainly distributed on the H atom of OH groups (see Fig. 1) [37]. Therefore, this study considered two directions for the binding of OA with PLA microparticles in chloroform and dichloromethane phases (see Fig. 2). It has been observed that the carboxylate group of OA interacts with the carboxylate group of PLA via C=O….H-O interactions, forming State I. This interaction occurs between the hydrogen and oxygen of both groups and has an E_{bin} value of -0.97 and -0.58 eV in the chloroform and dichloromethane environments, respectively. On the other hand, in State II, the hydrogen of the carboxylate group of OA interacts with the oxygen of the carbonyl group of PLA. The E_{bin} value for this interaction is 2.42 eV in the chloroform phase and -0.26 eV in the dichloromethane phase, as shown in Table 1. Assessment of the binding energies shows that the interaction of OA with PLA in State I is a chemical interaction in both phases, while State II in the chloroform phase is unstable and the complex has a weak interaction in the dichloromethane phase. Also, the thermodynamic function changes were calculated. The values of thermodynamic parameters for State I in the phases were calculated using B3LYP-D3/6-31+G** methods. The calculations revealed that in the chloroform phase, the enthalpy change (ΔH, kcal/mol), Gibbs free energy change (ΔG, kcal/mol), and entropy change (ΔS, cal mol^{-1} K^{-1}) were determined to be -16.96, -18.67, and 5.74, while in the dichloromethane phase, they were found to be -13.17, 0.052, and -44.34, respectively. The results showed that the thermodynamic function changes are negative, suggesting that this complex is thermodynamically stable [38]. Also, negative values of the thermodynamic parameters in State I represent an exothermic process, which confirms the binding energies results.

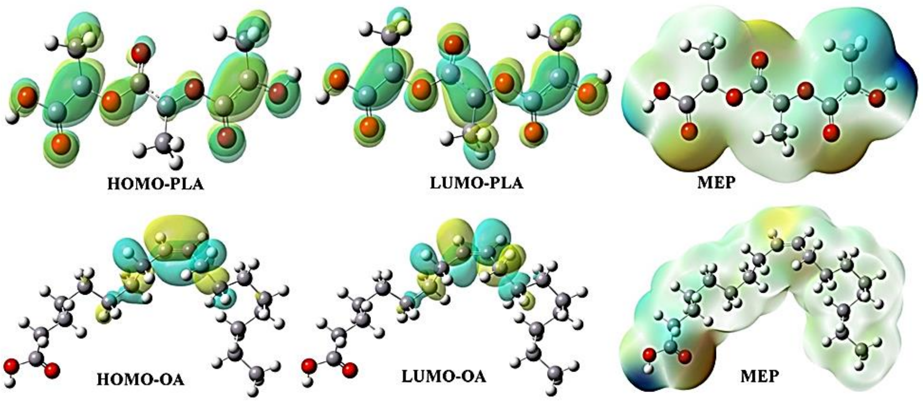

Fig. 1. HOMO/LUMO and MEP plots of oleic acid and PLA microparticles in chloroform phase
Рис. 1. Графики HOMO/LUMO и MEP микрочастиц олеиновой кислоты и PLA в фазе хлороформа

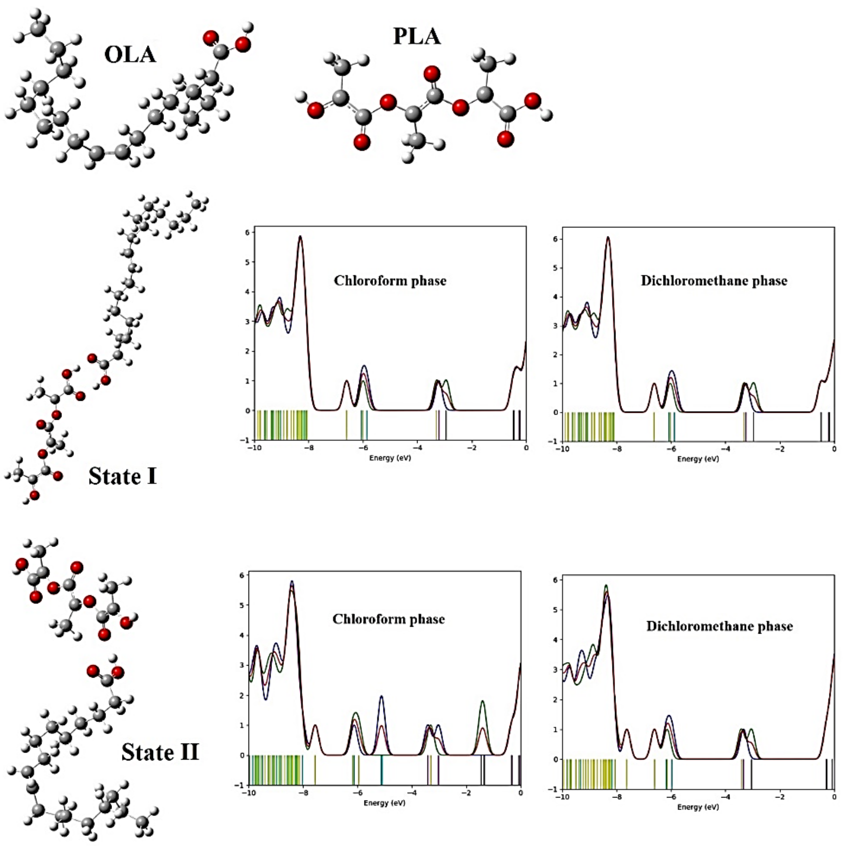

Fig. 2. Optimized structures of OA, PLA, and OA/PLA complexes and density of states of the complexes in chloroform and dichloromethane phases
Рис. 2. Оптимизированные структуры комплексов ОА, ПЛА и ОА/ПЛА и плотность состояний комплексов в хлороформной и дихлорметановой фазах

The values of dipole moment (DM) for pure PLA and OA molecules are 6.90 and 1.94 Debye in the chloroform phase and 7.34 and 2.07 Debye in the dichloromethane phase. After OA interacted with PLA, the DM values in States I and II were 5.60 and 5.92 Debye in the chloroform phase and 5.92 and 6.93 Debye in the dichloromethane phase. These changes in the DM values of the states, particularly in the chloroform phase, indicate an increased interaction of OA and PLA with non-polar solvents. This would lead to better dispersion and compatibility between the PLA matrix and the OA surfactant by increasing the internal molecular electric field. Therefore, the binding energies, thermodynamic parameters, and dipole moment results show that State I is more stable than State II in both phases, and the interaction of OA and PLA in this state is more likely and OA can be used as a suitable surfactant for PLA microparticle [39]. Fig. 3 also presents the MEP graphs for the states in the chloroform phase. As depicted in Fig. 3, states I and II show nearly gray areas. Put simply, the MEP of the complexes suggests that the oxygen atom of the carboxyl group targets the hydrogen atom of the hydroxyl group. This suggests a potential interaction between OA and PLA molecules in the complexes [40, 41].

The quantum molecular descriptors for the OA, PLA, and their complexes in the chloroform and dichloromethane environments are summarized in Table S1. Based on QMD analysis, each of these complexes shows little changes compared to the pure state in both phases which shows that interaction between OA and PLA molecules is possible in those complexes.

Table

Calculated binding energy (Ebin/eV), dipole moment (DM), HOMO energy (E_HOMO), LUMO energy (E_LUMO), energy gap (E_g) and Fermi level energy (E_F) for oleic acid, PLA, and their complexes in chloroform and dichloromethane phases

***Таблица.* Расчетная энергия связи (Ebin/эВ), дипольный момент (DM), энергия ВЗМО (E_HOMO), энергия LUMO (E_LUMO), энергетическая щель (E_g) и энергия уровня Ферми (E_F) для олеиновой кислоты, PLA и их комплексов в фазах хлороформа и дихлорметана**

Solvent	Property	$E_{bin/eV}$	E_{HOMO}/eV	E_{LUMO}/eV	E_g/eV	E_F/eV	$DM/Debye$
Chloroform	Oleic acid	-	-6.61	-0.34	6.27	-3.48	1.94
	PLA	-	-5.86	-3.21	2.65	-4.54	6.90
	State I	-0.97	-5.86	-3.21	2.65	-4.54	5.60
	State II	2.42	-5.10	-3.41	1.69	-4.26	5.92
Dichloromethane	Oleic acid	-	-6.62	-0.35	6.27	-3.49	2.07
	PLA	-	-5.86	-3.24	2.62	-4.55	7.34
	State I	-0.58	-5.87	-3.24	2.63	-4.56	5.97
	State II	-0.26	-5.97	-3.33	2.64	-4.65	6.83

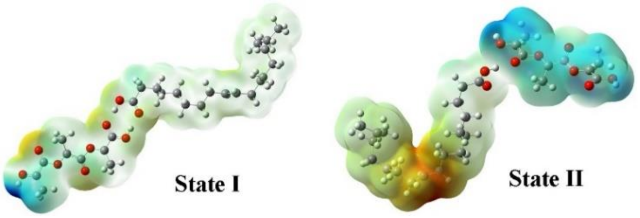

Fig. 3. The MEP of oleic acid with PLA microparticle in the chloroform phase

Рис. 3. МЭП олеиновой кислоты с микрочастицей PLA в фазе хлороформа

Electronic properties

Fig. 4 demonstrates the OA interacting with the PLA microparticle on the HOMO and LUMO wavefunctions in the chloroform phase. In State I, the HOMO and LUMO orbitals are localized on the C-C and C=O bonds of the PLA. On the other hand, in state II, the HOMO orbital is more localized on the C=C bonds of the surfactant. Conversely, the LUMO orbital is primarily concentrated on the C-C and C=O bonds of the microparticle, as well as the C=C bonds of the surfactant. The calculated HOMO and LUMO energies for the OA were found to be -6.61 and -0.34 eV, respectively. In the chloroform phase, the corresponding energies for the PLA microparticle were -5.86 and -3.21 eV, respectively, in that order. According to the overall density of the state (Table), the band gap (Eg) and Fermi level (E_F) values in State I and II show slight changes in comparison to the pure microparticle. The results show that there is an interaction between OA and PLA molecules.

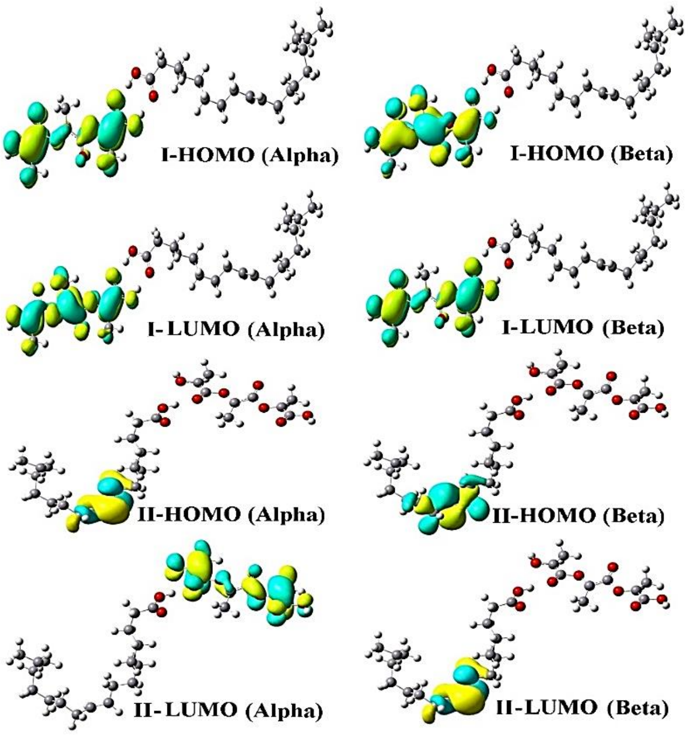

Fig. 4. HOMO/LUMO plots oleic acid with PLA microparticle in chloroform phase (state I and II)

Рис. 4. Графики HOMO/LUMO олеиновой кислоты с микрочастицами PLA в фазе хлороформа (состояния I и II)

UV-Vis analysis

The electronic absorption spectrum” of the considered system was calculated using the TD–DFT method. Theoretical analysis indicated that the PLA microparticle exhibits maximum absorption peaks at 212, 227, and 581 nm, which corresponds closely to the calculated absorption peaks observed in the experimental data (231 nm) [42]. In state I, the highest absorption peak is observed at 603 nm, with an oscillator strength (f) value of 0.36. Additionally, significant peaks are observed at 219 and 234 nm, with respective f values of 0.10 and 0.13. State II shows a maximum absorption peak at 584 nm with *f* value of 0.30 and also at 661 and 232 nm with *f* value of 0.07 and 0.14 (see Fig. 5). These changes in absorption peaks of UV indicate a good interaction between OA and the PLA microparticle.

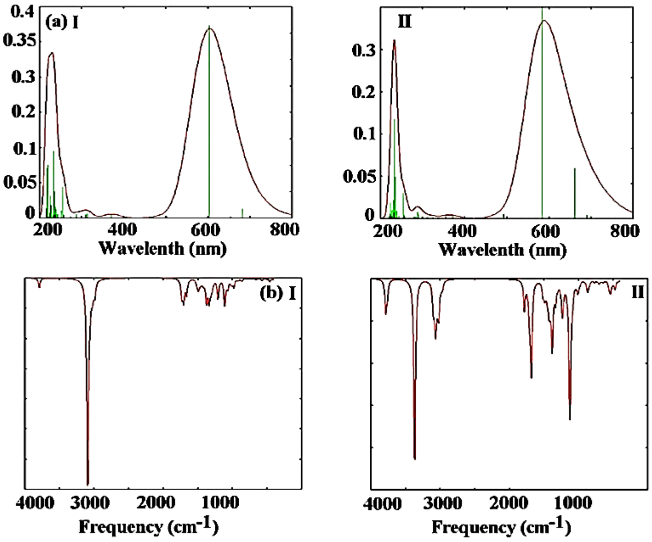

Fig. 5. Computed theoretical UV-vis and IR plots for OA with PLA microparticle in chloroform phase (state I and II)
Рис. 5. Рассчитанные теоретические УФ-Vis и ИК-графики ОА с микрочастицами PLA в фазе хлороформа (состояния I и II)

Infrared analysis

Fig. 5 displays the theoretical infrared (IR) curves of pure molecules and the interaction between OA and PLA in States I and II, within the chloroform phase. On the IR curve of pure PLA, the O-H bands are observed at 3763 and 3787 cm^{-1}, while the carbonyl bonds are seen at 1696 and 1715 cm^{-1}in the chloroform phase. Gadermann et al. [43] reported experimentally that the C=O stretching vibration of PLA polymer exhibited a frequency of 1758 cm^{-1}. The carbonyl bands of the OA interacting with PLA microparticle are visible at 1702, 1726, and 1738 cm^{-1} in State I, and at 1682, 1708, and 1737 cm^{-1} in State II. Additionally, the O-H groups are observed at 2988 cm^{-1} (OH of carboxylate groups) and 3790 cm^{-1} in State I, and at 3366, 3763, and 3787 cm^{-1} in State II. The decrease in the frequency of the OH bond in state I indicates a good interaction between the OH of the carboxylate group of PLA and the carbonyl bond of the carboxylate group of OA surfactant (O-H…C=O). These results are in very good agreement with the results of binding energies and dipole momentums.

CONCLUSION

The interaction of oleic acid (OA) as a surfactant with poly (lactic acid) (PLA) in the chloroform and dichloromethane phases was investigated using DFT and TDDFT methods at the B3LYP-D3/6-31+G** level of theory. The binding energies, thermodynamic parameters, and dipole moment results show that the interaction between OA and PLA via C=O….H-O interactions (state I) is a chemical interaction in both phases and the OA can be used as a suitable surfactant for PLA microparticles. The MEP graphs show that there is a possible interaction between OA and PLA molecules in the complexes. The QMD and electronic properties analysis exhibits slight changes in comparison to the pure PLA. The UV-Vis analysis and IR spectroscopy study indicate the interaction between OA and PLA. It appears that using the OA surfactant can improve dispersion and compatibility with the PLA matrix.

DECLARATION OF COMPETING INTEREST

The authors affirm that they have no known conflicting financial interests or personal relationships that could have influenced the work reported in this paper.

DATA AVAILABILITY

No data were utilized for the research described in the article.

The authors declare the absence a conflict of interest warranting disclosure in this article.

Авторы заявляют об отсутствии конфликта интересов, требующего раскрытия в данной статье.

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