Chem. Chem. Technol., 2025,
Vol. 19, No. 1, pp. 79–90

Chemistry

AMPHIPHILIC ESTERS OF PYROMELLITIC ACID: SYNTHESIS AND PROSPECTS OF APPLICATIONS

Volodymyr Donchak[1,✉], Andriy Voronov[2], Olha Budishevska[1], Ananiy Kohut[1], Yuriy Stetsyshyn[1]

https://doi.org/10.23939/chcht19.01.079

Abstract. This review focuses on amphiphilic diesters and "gemini" surfactants synthesized from pyromellitic acid, polyethylene glycols, aliphatic alcohols, and cholesterol. The discussion encompasses their unique colloidal and chemical properties, with an emphasis on the relationship between critical micelle concentration and hydrophilic-lipophilic balance. Structural factors, particularly the length of the lipophilic substituents, significantly influence CMC values in aqueous systems. Additionally, the presence of carboxyl groups in the pyromellitic acid core allows for pH-dependent modulation of surface activity. The amphiphiles exhibit exceptional potential in forming micellar structures capable of solubilizing hydrophobic substances, including dyes, oils, cholesterol, and the bioactive compound curcumin. Beyond enhancing the stability of these substances, they enable controlled release mechanisms that mimic cellular membrane interactions. Such versatility positions the materials from amphiphilic diesters of pyromellitic acid as promising candidates for innovative applications in targeted drug delivery systems and as nanoreactors for synthesizing silver nanoparticles. This review underscores their potential in advancing nanotechnology and biomedical engineering.

Keywords: pyromellitic acid, pyromellitic dianhydride, polyethylene glycol, cholesterol, gemini surfactants, solubilization, curcumin.

1. Introduction

In recent years, there has been increasing scientific and practical interest in amphiphilic reactive oligomers, which offer broad opportunities for modifying interfacial surfaces in various heterogeneous systems—such as polymer dispersions, filled composites, polymer blends, and planar surfaces. These modifications impart specific properties, including adjustable hydrophilicity, adhesive interactions, biocompatibility, and bactericidal activity. Amphiphilic oligomers are characterized by important colloidal and chemical properties, such as their ability to effectively reduce surface and interfacial tension through the adsorption and orientation of their molecules at phase boundaries. They also form hierarchical micellar structures of various sizes and shapes capable of solubilizing water-insoluble substances.

These unique properties make amphiphilic oligomers invaluable in numerous fields of modern science and technology, including the development of high-tech nanocomposites, "smart" polymer systems, efficient drug delivery platforms, and advanced disease diagnostic tools. The majority of amphiphilic oligomers are synthesized through radical copolymerization or polymer-analog transformations. However, drug delivery vehicles approved by the U.S. Food and Drug Administration (FDA) are predominantly obtained *via* polycondensation methods. A critical factor in the successful synthesis of such polycondensation-based oligomers is the use of multifunctional, highly reactive monomers.

One notable monomer is pyromellitic acid (PMA), which contains four reactive carboxyl groups in its molecule, enabling the construction of diverse structures by incorporating fragments with specific functional properties. PMA's availability, low cost, low toxicity, and easy transformation into reactive dianhydride make it a versatile building block for creating oligomeric and polymeric structures. These structures can be linear or branched, with varied functionality and solubility[1] as well as surfactants with tailored hydrophilic-lipophilic balance.[2-5]

Recently, various nanoassemblies, nanoparticles, and nanosponges based on dextrins and cyclodextrins crosslinked with pyromellitic dianhydride have been synthesized. These materials have been employed as innovative stimuli-responsive nanomaterials for drug delivery systems,[6] particularly for hydrophobic anticancer agents[7-9] as well as carriers for ailanthone-based herbicides,[10] anti-wrinkle finishing on cotton fabrics[11], *etc.*

This review focuses on the synthesis of novel amphiphilic derivatives of pyromellitic acid, examining

[1] Lviv Polytechnic National University, 12 S. Bandery St., Lviv 79013, Ukraine
[2] North Dakota State University, Dept. 2510, P.O. Box 6050, Fargo, ND 58108-6050, USA
✉ *volodymyr.a.donchak@lpnu.ua*

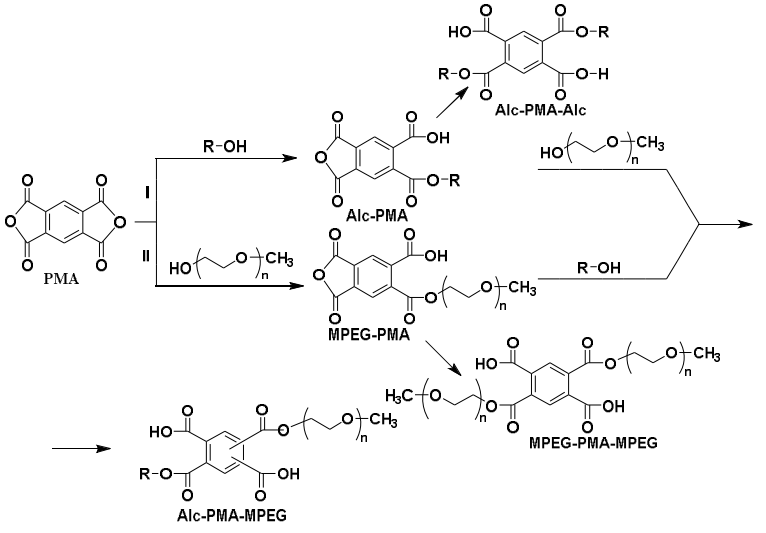
their physicochemical properties and versatile applications, including the solubilization of lipophilic substances in water and hydrophilic substances in non-polar solvents. Furthermore, it delves into their pivotal role in the development of modern nanoscale drug delivery systems and other advanced materials. Overall, the review underscores the increasing demand for innovative amphiphilic materials and their transformative impact on nanotechnology, biomedical applications, and cutting-edge scientific advancements.

2. Synthesis of the Amphiphilic Diesters of Pyromellitic Acid

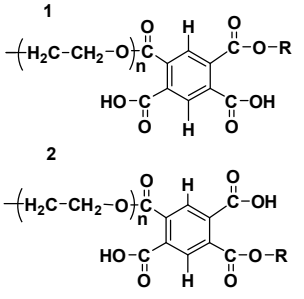
Amphiphilic diesters of pyromellitic acid (DEPMA) were synthesized through the sequential reaction of pyromellitic dianhydride (PMDA) with monomethylated polyethylene glycol (MPEG) and a primary aliphatic alcohol (R–OH), as depicted in Scheme 1. The incorporation of lipophilic alkyl or cholesteryl moieties alongside hydrophilic polyethylene glycol fragments enables the formation of self-assembled structures in aqueous media.[13] These self-associates can solubilize controlled amounts of lipophilic substances that are otherwise poorly soluble in water. The PEG chains, which constitute the hydrophilic shell of these self-associates, create a steric and hydrodynamic barrier that prevents aggregation. Moreover, the presence of PEG fragments renders these particles "invisible" to the immune system, facilitating prolonged and stable circulation in the bloodstream after injection.[13,14]

^{1}H NMR spectroscopy revealed that the primary product (Scheme 2) of the reaction between PMDA, MPEG, and alcohol is diester (2), with an estimated (2) to (1) ratio of approximately 7:3.

The synthesized DEPMAs exhibit amphiphilic properties, being soluble in both aqueous media and nonpolar solvents such as benzene, tetrachloroethane, chloroform, tetrahydrofuran, *etc.* This amphiphilicity arises from the simultaneous presence of both hydrophilic and lipophilic moieties in their molecular structure. Additionally, their surface activity, critical micelle concentration (CMC), and other colloidal-chemical properties depend on the pH of the medium due to the presence of carboxyl groups. Owing to these characteristics, DEPMA structures hold potential as nanocarriers for the solubilization and targeted delivery of lipophilic biologically active compounds and drugs to pathological cells *in vivo*.



Scheme 1. Synthesis of DEPMA (Alc-PMA-MPEG) by the interaction of PMDA with alcohols and MPEGs. R = Alc (But, Oct, Cet); n = 7, 12, 16



Scheme 2. Chemical structures of DEPMA (Alc-PMA-MPEG)

2.1. Amphiphilic Diesters with Cholesterol Fragments

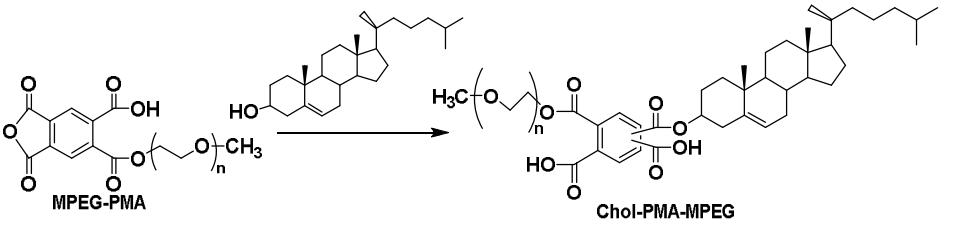
Oligomers containing cholesterol (Chol) moieties with the Chol-PMA-MPEG structure were synthesized according to Scheme 3 under conditions similar to those used for the synthesis of Alc-PMA-MPEG. However, the second stage required a slightly longer reaction time compared to the preparation of DEPMA with alkyl moieties. This was due to the lower reactivity of the secondary hydroxyl group in cholesterol relative to the primary hydroxyl group in aliphatic alcohols. The synthesis of Chol-PMA-MPEG was performed using an equimolar ratio of MPEG : PMDA : cholesterol.[15]

The selection of cholesterol as one of the lipophilic O-nucleophiles was motivated by its crucial role as a key component of cell membranes. Cholesterol exhibits a high thermodynamic affinity for membrane surfaces, influencing the stability and permeability of a double lipid layer.[16,17] Additionally, it regulates the activity of membrane-associated proteins, receptors, ion channels, *etc.*[18-20]

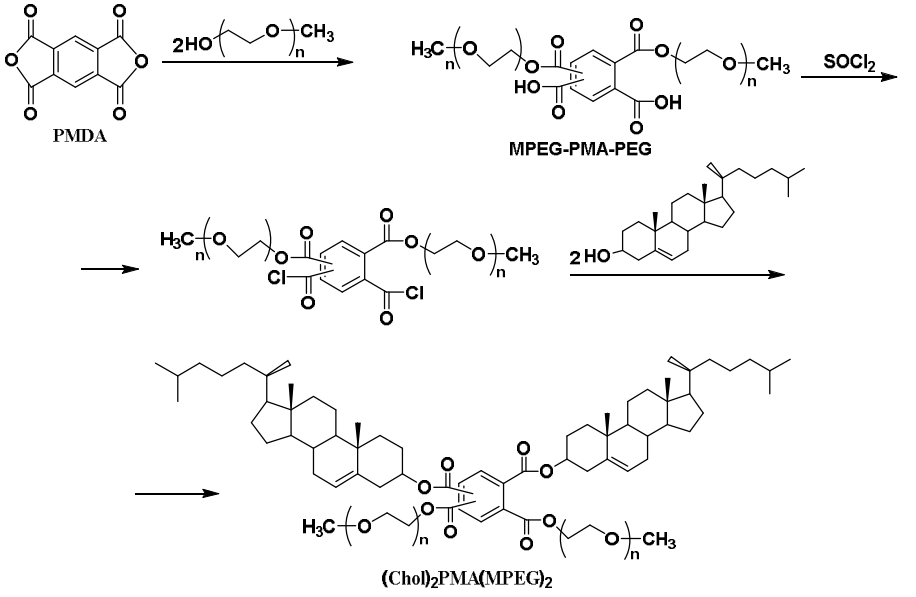
Water-soluble cholesterol derivatives are capable of self-assembly, leading to the formation of aggregates, micelles, and liquid crystalline phases.[21-26]

Polyethylene glycol (PEG) chains provide biocompatibility and bioinertness, resulting in minimal interaction with blood components, which makes them highly attractive for drug delivery applications.[27] Furthermore, the ester bonds in these oligomers can undergo gradual hydrolysis, yielding low-molecular-weight, non-toxic products that are naturally eliminated from the body.

Another class of amphiphilic surfactants, incorporating both polyethylene glycol and cholesterol moieties, was synthesized according to Scheme 4. These compounds, designated as $(MPEG)_2PMA(Chol)_2$, were obtained through a three-step synthetic procedure. In the first step, an acidic diester of pyromellitic acid (MPEG-PMA-MPEG) was synthesized, which was subsequently converted into a diacyl chloride intermediate. The final step involved the reaction of this intermediate with cholesterol, leading to the formation of $(MPEG)_2PMA(Chol)_2$.



Scheme 3. Synthesis of diesters with the Chol-PMA-MPEG structure



Scheme 4. Synthesis of diesters with the $(MPEG)_2PMA(Chol)_2$ structure

Unlike previous synthetic approaches, this method involved both anhydride groups of PMDA participating in the initial stage of the reaction. This allowed the process to be conducted under more stringent conditions, without the use of a solvent, enabling complete conversion of the starting materials at a stoichiometric ratio.

2.2. Amphiphilic Esters with a "Gemini" Structure

In recent years, a novel class of surfactants—dimeric or so-called "gemini" (also referred to as "double surfactants")—has gained significant attention from researchers and chemical industries.[28-30] These surfactants possess a symmetrical structure, consisting of two amphiphilic fragments linked by a spacer (Fig. 1).[31,32] Additionally, "gemini" surfactants without a spacer group have also been reported.[33]

Compared to conventional (monomeric) surfactants, "gemini" surfactants exhibit remarkably enhanced performance, making them some of the most promising surface-active compounds due to their amazing properties. They demonstrate superior wetting, foaming, solubilizing, and emulsifying properties, along with higher biological activity. Furthermore, they reduce surface tension at water–air and water–oil interfaces more effectively than their conventional counterparts.[34,35]

One of the key advantages of "gemini" surfactants is their significantly lower critical micelle concentration (CMC), which is typically at least an order of magnitude lower than that of corresponding monomeric surfactants. Additionally, their micelles exhibit a higher solubilization capacity. Studies of the microstructure of aqueous solutions of certain "gemini" surfactants have revealed that, at concentrations above the CMC, they can form micelles of various morphologies[36] depending on concentration,[37,38] temperature,[39] and the presence of other surfactants.[40,41] The morphology of these micelles includes worm-like,[42-44] thread-like,[45] and polymer-like structures.[46] Moreover, the "lifetime" of micelles formed by "gemini" surfactants is an order of magnitude longer than that of micelles formed by conventional surfactants.[47]

Due to their unique physicochemical properties, "gemini" surfactants have found widespread applications in diverse fields, including detergency,[48-53] soil and material wetting,[49] textile dyeing,[54-56] stabilization in microemulsion polymerization stabilization,[57] corrosion inhibition,[58,59] nanostructure formation,[60] oil spill remediation in natural water bodies,[61] gene transfection,[62,63] cosmetics formulation,[33] *etc*.

The synthesis of "gemini" surfactants based on pyromellitic acid and cholesterol is illustrated in Scheme 5.[12,16]

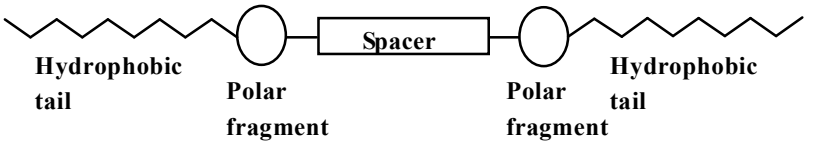
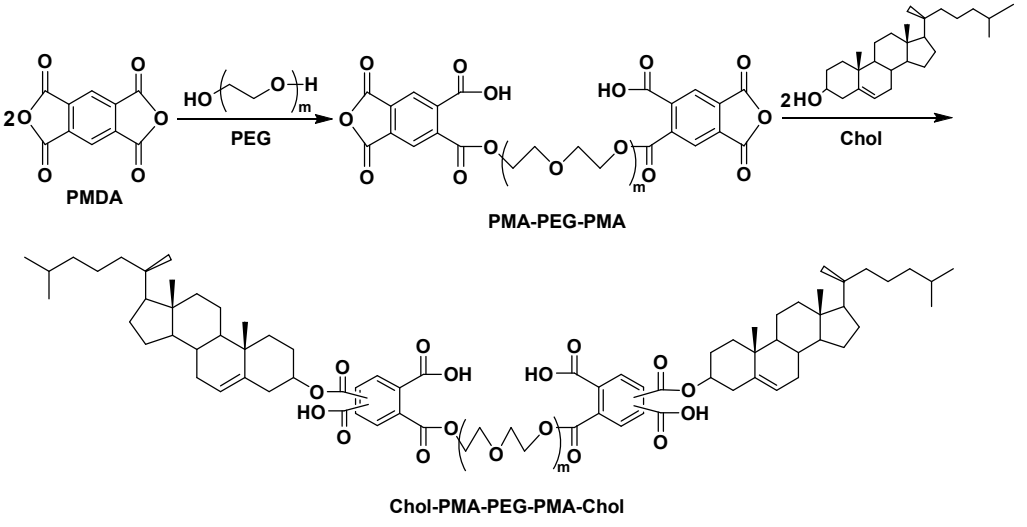


Fig. 1. Schematic representation of "gemini" surfactants



Scheme 5. Synthesis pathway of "gemini" Chol-PMA-PEG600-PMA-Chol oligomers

The synthesis consists of two stages. In the first step, the reaction of PMDA with PEG (in a molar ratio of 1:2) yields a PMA-PEG-PMA diester containing two anhydride groups (Scheme 5). In the second step, an excess of cholesterol undergoes acylation with this diester, wherein the hydroxyl groups of cholesterol react with the anhydride groups in PMA-PEG-PMA, leading to the formation of the final "gemini" surfactant structure.

3. Colloidal and Chemical Properties of Amphiphilic Diesters of Pyromellitic Acid

The synthesized diesters of pyromellitic acid (DEPMAs) exhibit amphiphilic properties, being soluble in both polar solvents, such as water, and low-polar organic solvents, including benzene, dioxane, tetrahydrofuran, chloroform, and tetrachloromethane. As previously mentioned, their amphiphilicity arises from the presence of one or two lipophilic moieties—either aliphatic primary alcohol residues or a cholesteryl group—along with one or two hydrophilic MPEG chains. The hydrophilic-lipophilic balance (HLB) of DEPMAs can be tuned within the range of 6.1 to 14.2 at the synthesis stage by varying the nature of the hydrophilic and lipophilic fragments.

When dissolved in water or an organic solvent, each DEPMA fragment undergoes solvation with solvent molecules of similar polarity. The coexistence of lipophilic and hydrophilic fragments determines surface activity and enables the formation of direct or reverse micelles and micellar aggregates, depending on the surrounding medium. The presence of two carboxyl groups in DEPMA's molecules allows for ionization in alkaline aqueous solutions, enhancing their hydrophilicity. Conversely, in an acidic medium, the reduced ionization of carboxyl groups increases the lipophilicity of the pyromellitic acid moiety. Consequently, the surface activity, HLB, and micelle-forming ability of DEPMAs in aqueous media are strongly pH-dependent.

The capacity to form both direct and reverse micelles enables the solubilization of water-insoluble lipophilic substances in aqueous media and water-soluble compounds in non-polar organic solvents. The critical micelle concentration (CMC) of DEPMAs, determined using the du Noüy ring method from surface tension isotherms, ranges from 0.02 to 1.22 wt. %. The CMC decreases with increasing lipophilic chain length and increases with longer hydrophilic chains. Remarkably, this trend is consistent across both acidic and neutral solutions.

On the other hand, CMC values obtained *via* fluorescence spectroscopy using pyrene as a fluorescent probe[64,65] range from 0.001 to 0.048 wt. %. This discrepancy suggests that the two methods characterize different aggregation processes in aqueous DEPMA solutions. The onset of pyrene solubilization corresponds to the concentration at which "unimeric micelles" capable of incorporating pyrene begin to form.[66] Meanwhile, surface tension isotherms reflect changes in interfacial energy at the water-air interface, indicating the DEPMA concentration at which a saturated adsorption layer is established at the interface. It is important to note that the affinity of the fluorescent probe for the micelle's lipophilic core influences the experimentally determined CMC values, which can therefore vary depending on the probe used.

The synthesized "gemini" oligomers also exhibit amphiphilic behavior, dissolving in both water and low-polar organic solvents such as benzene, dioxane, tetrahydrofuran, chloroform, and tetrachloromethane. This property results from the presence of a hydrophilic PEG chain and lipophilic cholesterol moieties in their structure. Similar to DEPMAs, the CMC values determined *via* the fluorescent probe method are lower than those obtained from surface tension measurements. Specifically, the formation of a saturated adsorption layer at the interface occurs at a "gemini" oligomer concentration of 0.01 wt. %, whereas pyrene solubilization begins at just 0.0007 wt. %.

The sizes of micelles and their aggregates in aqueous DEPMA colloidal solutions were examined using dynamic light scattering (DLS) at 25°C and pH 6.5 ± 0.3. At concentrations below the CMC (as determined by the fluorescence probe method), dispersed particles ranging from 2 to 10 nm in diameter were observed. Upon reaching the CMC, micelles with a relatively narrow size distribution formed, with an average diameter of 70–100 nm for Cet-PMA-MPEG550 and 40–50 nm for Chol-PMA-MPEG550. As the concentration increased further, micelle sizes expanded to 250 nm and 60–70 nm, respectively, accompanied by a broader size distribution, indicating aggregate formation.

Similar trends were observed in the DLS analysis of aqueous colloidal solutions of the "gemini" oligomers. At concentrations below the CMC (0.0001 wt. %), Chol-PMA-PEG600-PMA-Chol formed unimodal particles (polydispersity index = 1.18) with an average diameter of approximately 14 nm. When the concentration increased to 0.0003 wt. %, the unimodal distribution persisted, and the average particle diameter increased to 100 nm. Further concentration increases led to greater polydispersity of the micelles.

3.1. Study of Lipophilic Substance Solubilization in Water

In the production of cosmetics and pharmaceuticals, a critical challenge is the formation of stable colloidal systems, particularly emulsions of water-

insoluble substances such as dyes, oils, vitamins, hydrocarbons, *etc.* To achieve this, surfactants are required that can efficiently solubilize lipophilic compounds in an aqueous medium, stabilize emulsions, remain non-toxic, and gradually degrade within the human body. Khomenko *et al.* studied the solubilization of various lipophilic substances – including the dye Nile Red (NR), oils, and cholesterol – within micelles or micellar aggregates formed by DEPMA.[67]

Solubilization of NR occurs at DEPMA concentrations exceeding the critical micelle concentration (CMC). The intensity of light absorption in colloidal solutions containing solubilized NR increases with increasing DEPMA concentration.

The efficiency of solubilization, defined as the ratio of solubilized substance to solubilizer (g of solubilized compound per g of surfactant), is influenced by micelle size and core characteristics, which depend on the chemical structure, hydrophilic-lipophilic balance (HLB), and nature of the lipophilic fragments in the surfactant.

As illustrated in Fig. 2, NR solubilization is significantly more effective in Cet-PMA-MPEG550 colloidal solutions compared to Oct-PMA-MPEG550. This difference can be attributed to the longer lipophilic chains in Cet-PMA-MPEG550, which contribute to a larger hydrophobic core capable of accommodating NR molecules more efficiently than Oct-PMA-MPEG550. Additionally, the presence of a lipophilic cholesteryl (Chol) moiety in the DEPMA structure enhances the solubilization capacity of micelles several times over compared to Cet-PMA-MPEG550 and Oct-PMA-MPEG550. This phenomenon is likely due to the structural similarity between the Chol moiety and NR.[27] For Chol-PMA-MPEG550, solubilization efficiency continues to increase with higher concentrations in aqueous colloidal solutions.

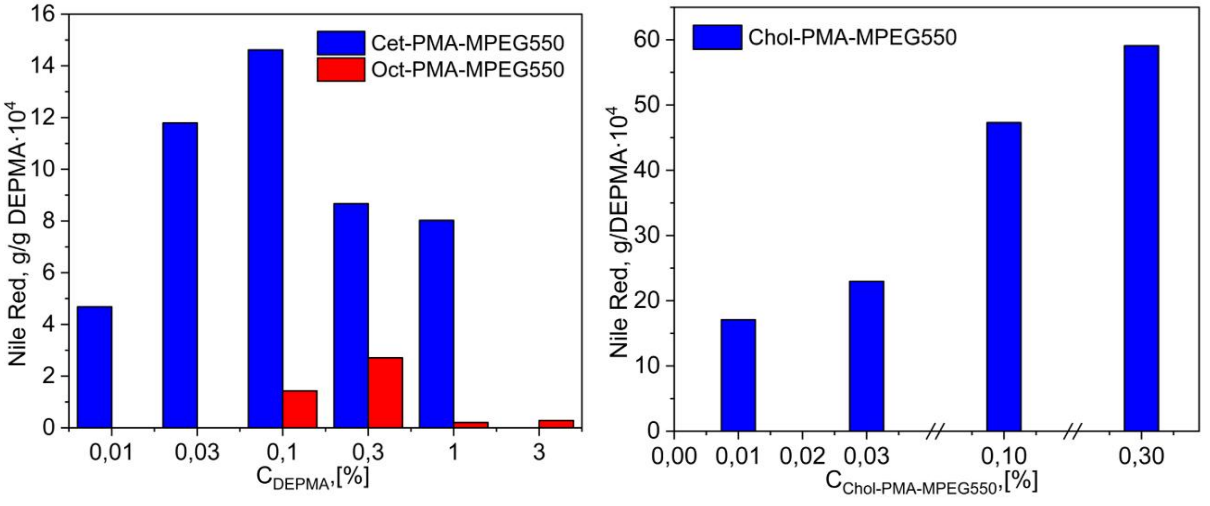


Fig. 2. Dependence of Nile Red solubilization efficiency on DEPMA concentration in aqueous colloidal solutions

Table 1. Efficiency of solubilization of lavender, orange, and fish oils in aqueous colloidal solutions of Cet-PMA-MPEG550 and Oct-PMA-MPEG550 at pH 8.2 and 8.4

DEPMA	Max. ratio of solubilized lavender oil to DEPMA, pH 8.2	Max. ratio of solubilized orange oil to DEPMA, pH 8.4	Max. ratio of solubilized fish oil to DEPMA, pH 8.4
Cet-PMA-MPEG550	2.386	0.016	0.008
Oct-PMA-MPEG550	1.430	0.021	0.010

Furthermore, a clear correlation is observed between solubilization efficiency and size of the micellar structures for Cet-PMA-MPEG550 and Oct-PMA-MPEG550. Larger micellar structures exhibit greater solubilization efficiency for NR, highlighting the role of micelle dimensions in accommodating lipophilic molecules.

The oils used as solubilizates—including lavender, orange, and fish oil—vary in composition, consisting of complex mixtures of substances with different molecular weights and structures.

A comparison of the maximum solubilization capacities of DEPMA for different oils reveals that the

solubilization efficiency for lavender oil is two orders of magnitude higher than that for orange oil and three orders of magnitude higher than that for fish oil (Table 1). This discrepancy is likely due to differences in the molecular composition and physicochemical properties of the oils.

The composition of lavender oil primarily consists of oxygen-containing compounds, including esters, alcohols, terpene oxides, and ketones. These substances can be partially immobilized in the peripheral region of the micelle, which is formed by MPEG550 fragments. The lipophilic components of lavender oil, such as monoterpenes, camphor, *etc.* are solubilized within the lipophilic core of the micelle. This explains the significantly higher solubilization efficiency observed for lavender oil.

The main constituents of orange oil (>90%), including limonene, citral, decanal, esters of aliphatic and terpene alcohols, sesquiterpene aldehydes, *etc.* are lipophilic. Consequently, they are solubilized exclusively within the lipophilic cores of the micelles. Similarly, fish oil, which consists of lipophilic triglycerides of higher fatty acids, is inherently incompatible with PEG chains and is therefore solubilized only within the lipophilic cores of the micelles and micellar aggregates. This results in considerably lower solubilization efficiency for fish oil as well.

A particularly noteworthy property of certain DEPMAs is their ability to solubilize cholesterol molecules. Currently, hypercholesterolemia is treated using drugs that lower blood cholesterol levels *via* various mechanisms.[68] However, the adverse side effects of most of these drugs limit their therapeutic applications.[69] It is well known that elevated cholesterol levels in human blood contribute to arterial blockage, increasing the risk of cardiovascular diseases and strokes.

A total cholesterol level below 200 mg/dL (5.17 mmol/L) is considered normal, while levels between 200 and 239 mg/dL (5.17–6.18 mmol/L) are classified as borderline high, and levels of 240 mg/dL (6.21 mmol/L) or higher are considered elevated.[70] Therefore, the search for and development of new drugs capable of reducing cholesterol levels, for instance, through partial solubilization, remains a highly relevant area in modern pharmacology.

Cholesterol-containing DEPMAs, namely Chol-PMA-MPEG550 and the "gemini" surfactant Chol-PMA-PEG600-PMA-Chol, were investigated as potential cholesterol solubilizers in aqueous media. Using the Amplex® Red Cholesterol Assay Kit,[71] Khomenko *et al.* demonstrated that Chol-PMA-PEG600-PMA-Chol micelles exhibit a high solubilization capacity, with a maximum cholesterol solubilization of 59 ± 2.2 wt. % relative to Chol-PMA-PEG600-PMA-Chol at a "gemini" surfactant concentration of $1.0 \cdot 10^{-4}$%.[67]

In contrast, the more hydrophilic DEPMA Chol-PMA-MPEG550 exhibits a lower solubilization ability, with a maximum cholesterol solubilization of 15 ± 0.3 wt. % at a DEPMA concentration of $3.0 \cdot 10^{-2}$%.

The ability of DEPMAs and "gemini" surfactants to undergo hydrolytic cleavage of the ester groups is an important factor for their potential biomedical applications.[72,73] Studies have shown that most polyester macromolecules are susceptible to hydrolytic degradation both *in vitro* and *in vivo*.[74]

As shown in Fig. 3, after seven days, the conversion of the ester groups in the Chol-PMA-MPEG550 molecules reaches 37 ± 4%, whereas, in the "gemini" molecules of the Chol-PMA-PEG600-PMA-Chol oligomer, it reaches 62 ± 3%. These findings are consistent with previously reported data on the hydrolysis of structurally similar polyesters.[75-77]

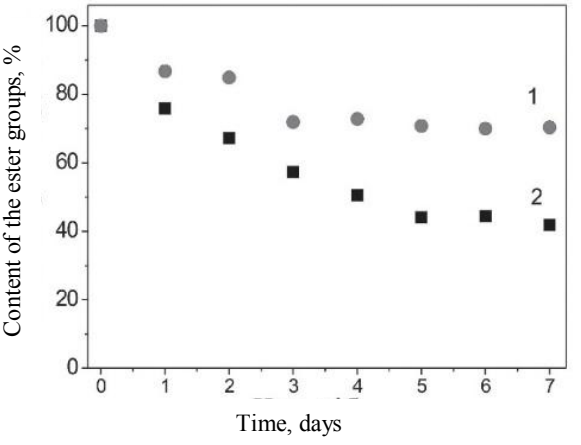


Fig. 3. Hydrolysis kinetics of Chol-PMA-MPEG550 (1) and "gemini" Chol-PMA-PEG600-PMA-Chol (2) in phosphate buffer (pH 7.0)

3.3. Study of Hydrophilic Substance Solubilization in Lipophilic Media

The synthesized DEPMAs can be utilized for the solubilization of water-soluble substances in lipophilic media. In particular, in benzene solutions of DEPMA, the benzene-insoluble dye malachite green (MG) forms a colloidal solution. The study found that at DEPMA concentrations exceeding the critical micelle concentration (Table 2), MG solubilization increases significantly due to the formation of reverse micelles.

These findings indicate that the synthesized DEPMAs belong to the class of invertible surfactants. In polar media, they form direct micelles with a hydrophilic shell and a lipophilic core, while in low-polarity solvents, they form reverse micelles with a lipophilic shell and a hydrophilic core.

Table 2. Critical micelle concentration (CMC) of DEPMA in benzene solutions

Lipophilic fragment	Hydrophilic fragment	CMC	
		mmol/L	%
$–C_4H_9$	MPEG550	11.9	1.0
$–C_8H_{17}$	MPEG350	33.5	2.3
$–C_8H_{17}$	MPEG550	10.6	0.95
$–C_8H_{17}$	MPEG750	4.9	0.53
$–C_{16}H_{33}$	MPEG550	9.2	0.93
$–C_{16}H_{33}$	MPEG750	4.8	0.58
-Chol	MPEG550	6.7	0.78

Consequently, the morphology, size, and core volume of both direct and reverse micelles, as well as micellar aggregates, are determined by the nature and proportion of hydrophilic and lipophilic fragments within the DEPMA molecules and their hydrophilic-lipophilic balance (HLB).

4. Nanosized Drug Delivery Systems

A pressing challenge in modern pharmacology is the development of nanoscale drug delivery systems for hydrophobic drugs targeted at pathological cells. To address this issue, amphiphilic polymers and oligomers capable of forming self-organized associates – such as micellar structures,[78-80] micro- and nanocapsules,[81] and liposomes[82] – are widely used. These systems not only solubilize a certain number of drug molecules but also protect them from rapid renal filtration and enzymatic degradation by proteases, esterases, and other enzymes, thereby extending their circulation time in the human body.[83]

It is well established that the therapeutic potential of many drugs prescribed for oncological, cardiovascular, and inflammatory diseases is severely limited by their low solubility in aqueous media. Consequently, the development of novel surfactants capable of solubilizing lipophilic, water-insoluble drugs is of critical importance for enhancing their colloidal solubility in aqueous solutions and for designing efficient drug delivery systems.[84,85] In this context, "gemini" surfactants – which are characterized by low CMC values and high solubilization capacity for a wide range of lipophilic substances – represent a promising platform for the development of such systems.

Micelles and micellar aggregates formed by DEPMAs and oligomers with a "gemini" structure exhibit a negative ζ-potential in the range of –10 to –60 mV across all studied concentrations. Negative ζ-potential is a crucial factor for using oligomers as nanocarriers for drug delivery, as it can potentially facilitate adhesion to gastrointestinal mucus and interaction with the cell surface, thereby promoting bioadhesion between the nanocarrier and intestinal epithelial cells.[86]

Curcumin is a bioactive compound with anti-inflammatory, antioxidant, antibacterial, and anticancer properties and is recommended for the treatment of a wide range of oncological, cardiovascular, and inflammatory diseases.[87] However, its practical insolubility in water significantly limits its bioavailability and therapeutic efficacy. The findings indicate that DEPMAs effectively solubilize curcumin within their micellar aggregates. The solubilization capacity for curcumin depends on the molecular structure of the DEPMA and generally increases with the length of its hydrophobic fragment, with Chol-PMA-MPEG550 demonstrating the highest efficiency.[88]

An important consideration is not only the ability of micelles to encapsulate curcumin within their hydrophobic cores – thus isolating it from the aqueous environment – but also their ability to prevent its degradation. Curcumin is known to be stable in acidic media, but it undergoes hydrolysis in neutral and alkaline conditions. For instance, in a pH 7.2 sodium phosphate buffer, over 90% of curcumin degrades within 30 minutes, forming ferulic acid, feruloylmethane, certain condensation products, and minor amounts of vanillin.[89]

In contrast, in a 0.2% micellar solution of Cet-PMA-MPEG550, only 32% of curcumin decomposes over 560 hours (23 days). This enhanced stability is likely attributed to the presence of acidic carboxyl groups within the micelle cores, where the majority of curcumin molecules are localized.[90]

To study the transport of solubilized hydrophobic drugs into cells, the water/1-octanol interface is commonly used as a model for the cell membrane.[89,91,92] The study examined the transfer of curcumin solubilized in Chol-PMA-MPEG550 and Cet-PMA-MPEG550 micelles from an aqueous solution (pH 6.5) into the oleophase of 1-octanol. After 48 hours, approximately 90% of the solubilized curcumin from Chol-PMA-MPEG550 and 100% from Cet-PMA-MPEG550 had successfully transferred into the oleophase.

These findings demonstrate that DEPMA micellar structures can serve as nanocontainers for curcumin in aqueous media, effectively stabilizing it for extended periods and facilitating its release at the water/oleophase interface. This highlights their potential for the development of novel drug delivery systems for lipophilic drugs and bioactive compounds, particularly curcumin.

5. Nanoreactors for the Synthesis of Silver Nanoparticles

Micellar structures formed by DEPMAs in benzene or chloroform have been utilized as nanoreactors for redox processes and the synthesis of nanosized silver particles.[93]

The formation of silver nanoparticles in the presence of surfactants containing polyoxyethylene chains occurs as a result of redox reactions involving oxyethylene units.[94]

Khomenko *et al.* have demonstrated that the number of silver nanoparticles formed in benzene solutions is directly proportional to the concentration of oxyethylene units within the micellar aggregates.[93] Consequently, in Oct-PMA-MPEG550 solutions, the yield of silver nanoparticles is significantly higher than in Oct-PMA-MPEG350 solutions, despite both having the same percentage concentration of DEPMA and the silver precursor $[Ag(NH_3)_2]OH$.

This suggests that a greater quantity of silver nanoparticles is produced within micellar aggregates that possess a larger total hydrophilic volume, which is attributed to the longer hydrophilic chains of MPEG550

6. Conclusions

A variety of amphiphilic biodegradable diesters and "gemini" oligomers based on pyromellitic acid have been developed, featuring hydrophilic fragments derived from polyethylene glycols PEG or monomethylated PEGs, and lipophilic fragments from aliphatic alcohols or cholesterol. The HLB and CMC of the synthesized surfactants are determined by the nature of their hydrophilic and hydrophobic fragments and can be tailored during synthesis. Above the CMC, resulting oligomers efficiently solubilize water-insoluble substances, including curcumin, a potent anticancer agent. Notably, the presence of carboxyl groups in the oligomers enhances curcumin's stability when solubilized within the micelles.

Surfactants containing cholesterol fragments demonstrate a unique ability to solubilize cholesterol in aqueous environments, offering potential for biomedical and pharmaceutical applications. Compared to other amphiphilic systems, such as those based on conventional surfactants or block copolymers, the tailored molecular design of resulting oligomers allows for greater control over their colloidal properties and cargo-loading efficiency.

DEPMA micellar nanomodalities exhibit physicochemical characteristics including tunable size distribution, chemical structure, and encapsulation capacity – that align with the requirements for efficient drug delivery. Their micellar hydrophobic cores enable the colloidal dissolution of lipophilic agents, while the hydrophilic exterior ensures stabilization in aqueous media. Moreover, in inverted micellar forms, DEPMA micellar nanomodalities can act as nanoreactors for the synthesis of silver nanoparticles, showcasing their versatility compared to traditional micellar systems.

References

[1] Alkan, B.; Daglar, O.; Luleburgaz, S.; Gungor, B.; Gunay, U.S.; Hizal, G.; Tunca, U.; Durmaz, H. One-Pot Cascade Polycondensation and Passerini Three-Component Reactions for the Synthesis of Functional Polyesters. *Polym. Chem.* **2022**, *13*, 258–266. https://doi.org/10.1039/D1PY01528A

[2] Koziel, K.; Lagiewka, J.; Girek, B.; Folentarska, A.; Girek, T.; Ciesielski, W. Synthesis of New Amino-β-Cyclodextrin Polymer, Cross-Linked with Pyromellitic Dianhydride and Their Use for the Synthesis of Polymeric Cyclodextrin Based Nanoparticles. *Polymers* **2021**, *13*, 1332. https://doi.org/10.3390/polym13081332

[3] Afinjuomo, F.; Barclay, T.; Song, Y.; Parikh, A.; Petrovsky, N.; Garg, S. Synthesis and Characterization of a Novel Inulin Hydrogel Crosslinked with Pyromellitic Dianhydride. *React. Funct. Polym.* **2019**, *134*, 104–111. https://doi.org/10.1016/j.reactfunctpolym.2018.10.014

[4] Arkas, M.; Vardavoulias, M.; Kythreoti, G.; Giannakoudakis, D.A. Dendritic Polymers in Tissue Engineering: Contributions of PAMAM, PPI PEG and PEI to Injury Restoration and Bioactive Scaffold Evolution. *Pharmaceutics* **2023**, *15*, 524. https://doi.org/10.3390/pharmaceutics15020524

[5] Polotti, G. Perspectives from Industry. *Adv. Chem. Eng.* **2020**, *56*, 259–330. https://doi.org/10.1016/bs.ache.2020.07.003

[6] Ciesielska, A.; Ciesielski, W.; Girek, B.; Girek, T.; Koziel, K.; Kulawik, D.; Lagiewka, J. Biomedical Application of Cyclodextrin Polymers Cross-Linked via Dianhydrides of Carboxylic Acids. *Appl. Sci.* **2020**, *10*, 8463. https://doi.org/10.3390/app10238463

[7] Peimanfard, S.; Zarrabi, A.; Trotta, F.; Matencio, A.; Cecone, C.; Caldera, F. Developing Novel Hydroxypropyl-β-Cyclodextrin-Based Nanosponges as Carriers for Anticancer Hydrophobic Agents: Overcoming Limitations of Host–Guest Complexes in a Comparative Evaluation *Pharmaceutics* **2022**, *14*, 1059. https://doi.org/10.3390/pharmaceutics14051059

[8] Monfared, Y.K.; Mahmoudian M.; Cecone, C.; Caldera, F.; Zakeri-Milani, P.; Matencio, A.; Trotta, F. Stabilization and Anticancer Enhancing Activity of the Peptide Nisin by Cyclodextrin-Based Nanosponges against Colon and Breast Cancer Cells. *Polymers* **2022**, *14*, 594. https://doi.org/10.3390/polym14030594

[9] Girek, T.; Koziel, K.; Girek, B.; Ciesielski, W. CD Oxyanions as a Tool for Synthesis of Highly Anionic Cyclodextrin Polymers. *Polymers* **2020**, *12*, 2845. https://doi.org/10.3390/polym12122845

[10] Demasi, S.; Caser, M.; Caldera, F.; Dhakar, N.K.; Vidotto, F.; Trotta, F.; Scariot, V. Functionalized Dextrin-Based Nanosponges as Effective Carriers for the Herbicide Ailanthone. *Ind. Crops Prod.* **2021**, *164*, 113346. https://doi.org/10.1016/j.indcrop.2021.113346

[11] Qi, H.; Meng, L.; Lin, X.; Xu, W.; Chen, Y.; Zhang, C.; Qiu, Y. Anti-Wrinkle Finishing of Cotton Fabrics with Pyromellitic Acid Enhanced by Polyol Extenders. *J. Donghua Univ. (Engl. Ed.)* **2022**, *39*, 533–541. https://doi.org/10.19884/j.1672-5220.202209006

[12] Tarnavchyk, I.; Voronov, A.; Donchak, V.; Budishevska, O.; Kudina, O.; Khomenko, O.; Harhay, K.; Samaryk, V.; Voronov, S. Synthesis and Selfassambling of Amphiphilic Oligoesters Based on Pyromellitic Acid. *Chem. Chem. Technol.* **2016**, *10*, 159–172. https://doi.org/10.23939/chcht10.02.159

[13] Müller, R.H. *Colloidal Carriers for Controlled Drug delivery and Targeting: Modification, Characterization and in Vivo Distribution*; CRC Press, 1991.

[14] Mishra, P.; Nayak, B.; Dey, R.K. PEGylation in Anti-Cancer Therapy: An Overview. *Asian J. Pharm. Sci.* **2016**, *11*, 337–348. https://doi.org/10.1016/j.ajps.2015.08.011

[15] Kudina, O.; Tarnavchyk, I.; Khomenko, O.; Budishevska, O.; Voronov, S.; Voronov, A. PEG and Cholesterol-Containing Pyromellitates: Synthesis and Self-Assembly. *Macromol. Chem. Phys.* **2013**, *214*, 2761–2767. https://doi.org/10.1002/macp.201300488
[16] Klok, H.-A.; Hwang, J.J.; Iyer, S.N.; Stupp, S.I. Cholesteryl-(L-Lactic Acid)$_n$ Building Blocks for Self-Assembling Biomaterials. *Macromolecules* **2002**, *35*, 746–759. https://doi.org/10.1021/ma010907x
[17] Heino, S.; Lusa, S.; Somerharju, P.; Ehnholm, C.; Olkkonen, V.M.; Ikonen, E. Dissecting the Role of the Golgi Complex and Lipid Rafts in Biosynthetic Transport of Cholesterol to the Cell Surface. *Proc. Natl. Acad. Sci. U.S.A.* **2000**, *97*, 8375–8380. https://doi.org/10.1073/pnas.140218797
[18] Klausen, T.K.; Hougaard, C.; Hoffmann, E.K.; Pedersen, S.F. Cholesterol Modulates the Molume-Regulated Anion Current in Ehrlich-Lettre Ascites Cells via Effects on Rho and F-Actin. *Am. J. Physiol. Cell Physiol.* **2006**, *291*, C757–C771. https://doi.org/10.1152/ajpcell.00029.2006
[19] Levitan, I.; Christian, A.E.; Tulenko, T.N.; Rothblat, G.H. Membrane Cholesterol Content Modulates Activation of Volume-Regulated Anion Current in Bovine Endothelial Cells. *J. Gen. Physiol.* **2000**, *115*, 405–416. https://doi.org/10.1085/jgp.115.4.405
[20] Maxfield, F.R.; Tabas, I. Role of Cholesterol and Lipid Organization in Disease. *Nature* **2005**, *438*, 612–621. https://doi.org/10.1038/nature04399
[21] Yusa, S. Self-Assembly of Cholesterol-Containing Water-Soluble Polymers. *Int. J. Polym. Sci.* **2012**, 609767. https://doi.org/10.1155/2012/609767
[22] Ringsdorf, H.; Schlarb, B.; Venzmer, J. Molecular Architecture and Function of Polymeric Oriented Systems: Models for the Study of Organization, Surface Recognition, and Dynamics of Biomembranes. *Angew. Chem. Int. Ed.* **1988**, *27*, 113–158. https://doi.org/10.1002/anie.198801131
[23] Zhou, Y.; Briand, V.A.; Sharma, N.; Ahn, S.; Kasi, R.M. Polymers Comprising Cholesterol: Synthesis, Self-Assembly, and Applications. *Materials* **2009**, *2*, 636–660. https://doi.org/10.3390/ma2020636
[24] Shibaev, V.P.; Platé, N.A.; Freidzon, Ya.S. Thermotropic Liquid Crystalline Polymers. I. Cholesterol-Containing Polymers and Copolymers. *J. Polym. Sci. Pol. Chem.* **1979**, *17*, 1655–1670. https://doi.org/10.1002/pol.1979.170170609
[25] Shibaev, V.P.; Tal'roze, R.V.; Karakhanova, F.I.; Platé, N.A. Thermotropic Liquid Crystalline Polymers. II. Polymers with Amino Acid Fragments in the Side Chains. *J. Polym. Sci. Pol. Chem.* **1979**, *17*, 1671–1684. https://doi.org/10.1002/pol.1979.170170610
[26] Yamaguchi, T.; Asada, T.; Hayashi, H.; Nakamura, N. Dependence of the Packing Structure of Mesogenic Groups on the Flexible Spacer Length of Liquid-Crystalline Side-Chain Polymers. *Macromolecules* **1989**, *22*, 1141–1144. https://doi.org/10.1021/ma00193a024
[27] Knop, K.; Hoogenboom, R.; Fischer, D.; Schubert, U.S. Poly(ethylene glycol) in Drug Delivery: Pros and Cons as Well as Potential Alternatives. *Angew. Chem. Int. Ed.* **2010**, *49*, 6288–6308. https://doi.org/10.1002/anie.200902672
[28] Menger, F.M.; Littau, C.A. Gemini Surfactants: Synthesis and Properties. *J. Am. Chem. Soc.* **1991**, *113*, 1451–1452. https://doi.org/10.1021/ja00004a077
[29] Menger, F.; Littau, C. Gemini Surfactants: A New Class of Self-Assembling Molecules. *J. Am. Chem. Soc.* **1993**, *115*, 10083–10090. https://doi.org/10.1021/ja00075a025
[30] Zana, R.; Xia, J. *Gemini Surfactants: Synthesis, Interfacial and Solution-Phase Behavior, and Applications*; Marcel Dekker, 2004.
[31] Sakai, K. Development of Commercially Available Gemini Surfactants. *J. Oleo Sci*. **2012**, *12*, 627–633. https://doi.org/10.5650/oleoscience.12.627
[32] Rosen, M.J. Geminis: A New Generation of Surfactants. *Chemtech* **1993**, *23*, 30–33.
[33] Villa, C.; Baldassari, S.; Martino, D.F.C.; Spinella, A.; Caponetti, E. Green Synthesis, Molecular Characterization and Associative Behavior of Some Gemini Surfactants without a Spacer Group. *Materials* **2013**, *6*, 1506–1519. https://doi.org/10.3390/ma6041506
[34] Zana, R. Gemini (Dimeric) Surfactants. *Curr. Opin. Colloid Interface Sci.* **1996**, *1*, 566–571. https://doi.org/10.1016/S1359-0294(96)80093-8
[35] Brycki, B.E.; Kowalczyk, I.H; Szulc, A.; Kaczerewska, O.; Pakiet, M. Multifunctional Gemini Surfactants: Structure, Synthesis, Properties, and Applications. In *Application and Characterization of Surfactants*; Intech World's Largest Science, Technology & Medicine Open Access Book Publisher, 2017.
[36] Song, B.; Hu, Y.; Song, Y.; Zhao, J. Alkyl Chain Length-Dependent Viscoelastic Properties in Aqueous Wormlike Micellar Solutions of Anionic Gemini Surfactants with an Azobenzene Spacer. *J. Colloid Interface Sci.* **2010**, *341*, 94–100. https://doi.org/10.1016/j.jcis.2009.09.023
[37] Ahmady, A. R.; Hosseinzadeh, P.; Solouk, A.; Akbari, S.; Szulc, A.M.; Brycki, B.E. Cationic Gemini Surfactant Properties, Its Potential as a Promising Bioapplication Candidate, and Strategies for Improving Its Biocompatibility: A Review. *Adv. Colloid Interface Sci.* **2022**, *299*, 102581. https://doi.org/10.1016/j.cis.2021.102581
[38] Pei, X.; Zhao, J.; Ye, Y.; You, Y; Wei, X. Wormlike Micelles and Gels Reinforced by Hydrogen Bonding in Aqueous Cationic Gemini Surfactant Systems. *Soft Matter* **2011**, *7*, 2953–2960. https://doi.org/10.1039/C0SM01071E
[39] Degiorgio, V.; Corti, M. *Physics of Amphiphiles: Micelles, Vesicles and Microemulsion*; North Holland Physics Publishing, 1985.
[40] Shrestha, R.G.; Shrestha, L.K.; Matsunaga, T.; Shibayama, M.; Aramaki, K. Lipophilic Tail Architecture and Molecular Structure of Neutralizing Agent for the Controlled Rheology of Viscoelastic Fluid in Amino Acid-Based Anionic Surfactant System. *Langmuir* **2011**, *27*, 2229–2236. https://doi.org/10.1021/la1048248
[41] Shrestha, R.G.; Abezgauz, L.; Danino, D.; Sakai, K.; Sakai, H.; Abe, M. Structure and Dynamics of Poly(oxyethylene) Cholesteryl Ether Wormlike Micelles: Rheometry, SAXS, and Cryo-TEM Studies. *Langmuir* **2011**, *27*, 12877–12883. https://doi.org/10.1021/la202879f
[42] Bhadani, A.; Shrestha, R.G.; Koura, S.; Endo, T.; Sakai, K.; Abe, M.; Sakai, H. Self-Aggregation Properties of New Ester-Based Gemini Surfactants and Their Rheological Behavior in the Presence of Cosurfactant – Monolaurin. *Colloids Surf. A: Physicochem. Eng. Asp.* **2014**, *461*, 258–266. https://doi.org/10.1016/j.colsurfa.2014.08.001
[43] Pei, X.; Xu, Z.; Song, B.; Cui, Z.; Zhao, J. Wormlike Micelles Formed in Catanionic Systems Dominated by Cationic Gemini Surfactant: Synergistic Effect with High Efficiency. *Colloids Surf. A: Physicochem. Eng. Asp.* **2014**, *443*, 508–514. https://doi.org/10.1016/j.colsurfa.2013.12.007
[44] Lin, Z.; Scriven, L.E.; Davis, H.T. Cryogenic Electron Microscopy of Rodlike or Wormlike Micelles in Aqueous Solutions

of Nonionic Surfactant Hexaethylene Glycol Monohexadecyl Ether. *Langmuir* **1992**, *8*, 2200–2205. https://doi.org/10.1021/la00045a021
[45] Vinson, P.K.; Talmon, Y. Comments on "Electron Diffraction Observed in the Gigantic Micelle-Producing System of CTAB-Aromatic Additives," by Hirata, Sakaiguchi, and Akai. *J. Colloid Interface Sci.* **1989**, *133*, 288–289. https://doi.org/10.1016/0021-9797(89)90305-6
[46] Jerke, G.; Pedersen, J.S.; Egelhaaf, S.U.; Schurtenberger, P. Flexibility of Charged and Uncharged Polymer-Like Micelles. *Langmuir* **1998**, *14*, 6013–6024. https://doi.org/10.1021/la980390r
[47] Groth, C.; Nydén, M.; Holmberg, K.; Kanicky, J.R.; Shah, D.O. Kinetics of the Self-Assembly of Gemini Surfactants. *J. Surfactants Deterg.* **2004**, *7*, 247–255. https://doi.org/10.1007/s11743-004-0308-8
[48] Rosen, M.J.; Tracy, D.J. Gemini Surfactants. *J. Surfactants Deterg.* **1998**, *1*, 547–554. https://doi.org/10.1007/s11743-998-0057-8
[49] Micich, T.J.; Linfield, W.M. Wetting Properties of Nonionics from Branched Fatty Diamides. *J. Am. Oil Chem. Soc.* **1988**, *65*, 820–825. https://doi.org/10.1007/BF02542540
[50] Quencer, L.B.; Kokke-Hall, S.; Loughney, T. Proceedings of CESIO 4th World Surfactant Congress. **1996**, *2*, 66.
[51] Kumar, N.; Tyagi, R. Industrial Applications of Dimeric Surfactants: A Review. *J. Dispers. Sci. Technol.* **2014**, *35*, 205–214. https://doi.org/10.1080/01932691.2013.780243
[52] Rosen, M.J. Gemini Surfactants. *Industrial Applications of Surfactants IV* **1999**, 151–161. https://doi.org/10.1533/9781845698614.151
[53] Li, J.; Dahanayake, M.; Reierson, R.L.; Tracy, D.J. Amphoteric Surfactants Having Multiple Hydrophobic and Hydrophilic Groups. US patent 5,914,310, June 22, 1999.
[54] Choi, T.-S.; Shimizu, Y.; Shirai, H.; Hamada, K. Disperse Dyeing of Nylon 6 Fiber Using Gemini Surfactants Containing Ammonium Cations as Auxililiaries. *Dyes Pigments* **2001**, *48*, 217–226. https://doi.org/10.1016/S0143-7208(00)00105-4
[55] Choi, T.-S.; Shimizu, Y.; Shirai, H.; Hamada, K. Disperse Dyeing of Polyester Fiber Using Gemini Surfactants Containing Ammonium Cations as Auxililiaries. *Dyes Pigments* **2001**, *50*, 55–65. https://doi.org/10.1016/S0143-7208(01)00033-X
[56] Choi, T.-S.; Shimizu, Y.; Shirai, H.; Hamada, K. Solubilization of Disperse Dyes in Cationic Gemini Surfactant Micelles. *Dyes Pigments* **2000**, *45*, 145–152. https://doi.org/10.1016/S0143-7208(00)00015-2
[57] Dreja, M.; Tieke, B. Polymerization of Styrene in Ternary Microemulsion Using Cationic Gemini Surfactants *Langmuir* **1998**, *14*, 800–807. https://doi.org/10.1021/la9710738
[58] El-Sadek, B.M. Synthesis of Selected Gemini Surfactants: Surface, Biological Activity and Corrosion Efficiency against Hydrochloric Acid Medium. *Der Chemica Sinica* **2011**, *2*, 125–137.
[59] Mobin, M.; Masroor, S. Cationic Gemini Surfactants as Novel Corrosion Inhibitor for Mild Steel in 1M HCl. *Int. J. Electrochem. Sci.* **2012**, *7*, 6920–6940. https://doi.org/10.1016/S1452-3981(23)15758-0
[60] Chen, X.; Wang, J.; Shen, N.; Luo, Y.; Li, L.; Liu, M.; Thomas, R.K. Gemini Surfactant/DNA Complex Monolayers at the Air−Water Interface: Effect of Surfactant Structure on the Assembly, Stability and Topography of Monolayers. *Langmuir* **2002**, *18*, 6222–6228. https://doi.org/10.1021/la025600l
[61] Yan, X.; Janout, V.; Regen, S.L. Hydrophobic Sponges: Resin-Bound Surfactants as Organic Scavengers. *Macromolecules* **2002**, *35*, 8243–8246. https://doi.org/10.1021/ma020568n
[62] Fielden, M.L.; Perrin, C.; Kremer, A.; Bergsma, M.; Stuart, M.C.; Camilleri, P.; Engberts, J.B.F.N. Sugar-Based Tertiary Amino Gemini Surfactants with a Vesicle-to-Micelle Transition in the Endosomal pH Range Mediate Efficient Transfection *in vitro*. *Eur. J. Biochem.* **2001**, *268*, 1269–1279. https://doi.org/10.1046/j.1432-1327.2001.01995.x
[63] Buijnsters, P.J.J.A.; Rodríguez, C.L.G.; Willighagen, E.L.; Sommerdijk, N.A.J.M.; Kremer, A.; Camilleri, P.; Feiters, M.C.; Nolte, R.J.M.; Zwanenburg, B. Cationic Gemini Surfactants Based on Tartaric Acid: Synthesis, Aggregation, Monolayer Behaviour, and Interaction with DNA. *Eur. J. Org. Chem.* **2002**, *2002*, 1397–1406. https://doi.org/10.1002/1099-0690(200204)2002:8<1397::AID-EJOC1397>3.0.CO;2-6
[64] Wilhelm, M.; Zhao, C.L.; Wang, Y.; Xu, R.; Winnik, M.A.; Mura, J.L.; Riess, G.; Croucher, M.D. Poly(Styrene-Ethylene Oxide) Block Copolymer Micelle Formation in Water: A Fluorescence Probe Study. *Macromoleules* **1991**, *24,* 1033–1040. https://doi.org/10.1021/ma00005a010
[65] Schmitz, C.; Mourran, A.; Keul, H.; Möller, M. Synthesis and Association Behaviour of Linear Block Copolymers with Different Microstructures but the Same Composition. *Macromol. Chem. Phys.* **2008**, *209*, 1859–1971. https://doi.org/10.1002/macp.200800205
[66] Matsuoka, H.; Matsutani, M.; Mouri, E.; Matsumoto, K. Polymer Micelle Formation without Gibbs Monolayer Formation: Synthesis and Characteritics of Amphiphilic Diblock Copolymer Having Strong Acid Groups. *Macromolecules* **2003**, *36*, 5321–5330. https://doi.org/10.1021/ma0215161
[67] Khomenko, O.; Budishevska, O.; Voronov, A.; Varvarenko, S.; Kudina, O.; Tarnavchyk, I.; Voronov, S. Amphiphilic Diesters of Pyromellitic Acid with Cholesterol Fragments for Solubilization of Lipophilic Substances. *Reports of the National Academy of Sciences of Ukraine* **2013**, *7*, 123–129. http://dspace.nbuv.gov.ua/handle/123456789/85809
[68] Suckling, K.E.; Benson, G.M.; Bond, B.; Gee, A.; Glen, A.; Haynes, C.; Jackson, B. Cholesterol Lowering and Bile Acid Excretion in the Hamster with Cholestyramine Treatment. *Atherosclerosis* **1991**, *89*, 183–190. https://doi.org/10.1016/0021-9150(91)90059-C
[69] Mol, M.J.T.M.; Erkelens, D.W.; Leuven, J.A.G.; Schouten, J.A.; Stalenhoef, A.F.H. Simvastatin (MK-733): A Potent Cholesterol Synthesis Inhibitor in Heterozygous Familial Hypercholesterolaemia. *Atherosclerosis* **1988**, *69*, 131–137. https://doi.org/10.1016/0021-9150(88)90006-8
[70] Rosenson, R. Patient education: High Cholesterol and Lipids (Beyond the Basics). *UpToDate*. **2024, Sep 27.** UpToDate Inc. www.uptodate.com.
[71] Molecular probes. Amplex® RedCholesterolAssayKitCatalogno. A12216.
[72] Okada, H.; Toguchi, H. Biodegradable Microspheres in Drug Delivery. *Crit. Rev. Ther. Drug Carrier Syst.* **1995**, *12*, 1–99. https://doi.org/10.1615/CritRevTherDrugCarrierSyst.v12.i1.10
[73] Scott, G.; Gilead, D. *Degradable Polymers, Principles and Applications*; Chapman & Hall, 1995.
[74] Anderson, J.M.; Shive, M.S. Biodegradation and Biocompatibility of PLA and PLGA Microspheres. *Adv. Drug Deliv. Rev.* **2002**, *64*, 72–82. https://doi.org/10.1016/j.addr.2012.09.004
[75] Grizzi, I.; Garreau, H.; Li, S.; Vert, M. Hydrolytic Degradation of Devices Based on Poly(DL-Lactic Acid) Size-Dependence. *Biomaterials* **1995**, *16*, 305–311. https://doi.org/10.1016/0142-9612(95)93258-F

[76] Vert, M.; Li, S.M.; Garreau, H. Attempts to Map the Structure and Degradation Characteristics of Aliphatic Polyesters Derived from Lactic and Glycolic Acids. *J. Biomater. Sci. Polym. Ed.* **1995**, *6*, 639–649. https://doi.org/10.1163/156856294X00581
[77] Vert, M.; Li, S. M.; Garreau, H. Recent Advances in the Field of Lactic Acid/Glycolic Acid Polymer-Based Therapeutic Systems. *Macromol. Symp*. **1995**, *98*, 633–642. https://doi.org/10.1002/masy.19950980154
[78] Huh, K.M.; Min, H.S.; Lee, S.C.; Lee, H.J.; Kim, S.; Park, K. A New Hydrotropic Block Copolymer Micelle System for Aqueous Solubilization of Paclitaxel. *J. Control. Release* **2008**, *126*, 122–129. https://doi.org/10.1016/j.jconrel.2007.11.008
[79] Konno, T.; Junji, W.; Ishihara, K. Enhanced Solubility of Paclitaxel Using Water-Soluble and Biocompatible 2-Methacryloyloxyethyl Phosphorylcholine Polymers. *J. Biomed. Mater. Res. - A* **2003**, *65A*, 209–214. https://doi.org/10.1002/jbm.a.10481
[80] Kim, S.C.; Kim, D.W.; Shim, Y.H.; Bang, J.S.; Oh, H.S.; Kim, S.W.; Seo, M.H. In Vivo Evaluation of Polymeric Micellar Paclitaxel Formulation: Toxicity and Efficacy. *J. Control. Release* **2001**, *72*, 191–202. https://doi.org/10.1016/S0168-3659(01)00275-9
[81] Desai, N.P.; Trieu, V.; Hwang, L.Y.; Wu, R.; Soon-Shiong, P.; Gradishar, W.J. Improved Effectiveness of Nanoparticle Albumin-Bound (NAB) Paclitaxel Versus Polysorbate-Based Docetaxel in Multiple Xenografts as a Function of HER2 and SPARC Status. *Anti-Cancer Drugs* **2008**, *19*, 899–909. https://doi.org/10.1097/CAD.0b013e32830f9046
[82] Wu, J.; Liu, Q.; Lee, R.J. A Folate Receptor-Targeted Liposomal Formulation for Paclitaxel. *Int. J. Pharm.* **2006**, *316*, 148–153. https://doi.org/10.1016/j.ijpharm.2006.02.027
[83] Litzinger, D.C.; Huang, L. Phosphatodylethanolamine Liposomes: Drug Delivery, Gene Transfer and Immunodiagnostic Applications. *Biochim. Biophys. Acta, Rev. Biomembr*. **1992**, *1113*, 201–227. https://doi.org/10.1016/0304-4157(92)90039-D
[84] Sinha, R.; Kim, G.J.; Nie, S.; Shin, D.M. Nanotechnology in Cancer Therapeutics: Bioconjugated Nanoparticles for Drug Delivery. *Mol. Cancer Ther*. **2006**, *5*, 1909–1917. https://doi.org/10.1158/1535-7163.MCT-06-0141
[85] Sakamoto, J.H.; van de Ven, A.L.; Godin, B.; Blanco, E.; Serda, R.E.; Grattoni, A.; Ziemys, A.; Bouamrani, A.; Hu, T.; Ranganathan, S.I. *et al.* Enabling Individualized Therapy through Nanotechnology. *Pharmacol. Res*. **2010**, *62*, 57–89. https://doi.org/10.1016/j.phrs.2009.12.011
[86] Lo, C.-L.; Lin, K.-M.; Huang, C.-K.; Hsiue, G.-H. Self-Assembly of a Micelle Structure from Graft and Diblock Copolymers: An Example of Overcoming the Limitations of Polyions in Drug Delivery. *Adv. Funct. Mater*. **2006**, *16*, 2309–2316. https://doi.org/10.1002/adfm.200500627
[87] Anand, P.; Kunnumakkara, A.B.; Newman, R.A. Aggarwal, B.B. Bioavailability of Curcumin: Problems and Promises. *Mol. Pharmaceutics* **2007**, *4*, 807–818. https://doi.org/10.1021/mp700113r
[88] Demchuk, Z.; Savka, M.; Voronov, A.; Budishevska, O.; Donchak, V.; Voronov, S. Amphiphilic Polymers Containing Cholesterol for Drug Delivery Systems. *Chem. Chem. Technol*. **2016**, *10*, 561–570. https://doi.org/10.23939/chcht10.04si.561
[89] Kumar, A.; Ahuja, A.; Ali, J.; Baboota, S. Conundrum and Therapeutic Potential of Curcumin in Drug Delivery. *Crit. Rev. Ther. Drug Carrier Syst*. **2010**, *27*, 279–312. https://doi.org/10.1615/CritRevTherDrugCarrierSyst.v27.i4.10
[90] Khomenko, O.; Budishevska, O.;Voronov, A.; Kudina, O.; Tarnavchyk, I.; Voronov, S. Amphiphilic Oligomers Based on Diesters of Pyromellitic Acid for the Solubilization of Lipophilic Agents. *Int. J. Theor. Appl. Nanotechnol*. **2013**, *1*, 17–25. https://doi.org/10.11159/ijtan.2013.002
[91] *Lipophilicity in Drug Action and Toxicology*; Plišca, V.; Testa, B.; van de Waterbeemd, H., Eds.; VCH: Weinheim, 1996.
[92] Popadyuk, N.; Zholobko, O.; Donchak, V.; Harhay, K.; Budishevska, O.; Voronov, A.; Kohut, A.; Voronov, S. Ionically and Covalently Crosslinked Hydrogel Particles Based on Chitosan and Poly(Ethylene Glycol). *Chem. Chem. Technol*. **2014**, *8*, 171–176. https://doi.org/10.23939/chcht08.02.171
[93] Khomenko, O.; Budishevska, O; Varvarenko, S.; Voronov, A.; Kudina, O.; Chekailo, M.; Voronov, S. Micellar structures of amphiphilic diesters of pyromellitic acid for the synthesis of silver nanoparticles. *Bulletin of the National University "Lviv Polytechnic" series: "Chemistry, technology of substances and their applications"* **2012**, *726,* 332–340.
[94] Voronov, A.; Kohut, A.; Vasylyev, S.; Peukert, W. Mechanism of Silver Ion Reduction in Concentrated Solutions of Amphiphilic Invertible Polyesters in Nonpolar Solvent at Room Temperature. *Langmuir* **2008**, *24*, 12587–12594. https://doi.org/10.1021/la801769v

Received: October 01, 2024 / Revised: October 14, 2024 / Accepted: November 08, 2024

АМФІФІЛЬНІ ЕСТЕРИ ПІРОМЕЛІТОВОЇ КИСЛОТИ: СИНТЕЗ І ПЕРСПЕКТИВИ ЗАСТОСУВАННЯ

Анотація. *Цей огляд присвячений амфіфільним діестерам і поверхнево-активним «геміні»-речовинам, синтезованим з піромелітової кислоти, поліетиленгліколів, аліфатичних спиртів і холестеролу. Обговорення охоплює їхні унікальні колоїдні та хімічні властивості, з акцентом на взаємозв'язку між критичною концентрацією міцелоутворення (ККМ) і гідрофільно-ліпофільним балансом. Структурні фактори, зокрема довжина ліпофільних замісників, значно впливають на величину ККМ у водних системах. Крім того, наявність карбоксильних груп у фрагменті піромелітинової кислоти дає змогу здійснювати pH-залежну модуляцію поверхневої активності. Описані амфіфільні речовини мають винятковий потенціал у формуванні міцелярних структур, здатних солюбілізувати гідрофобні речовини, зокрема барвники, олії, холестерол і біологічно активну речовину куркумін. Окрім підвищення стабільності цих речовин, вони забезпечують механізми контрольованого вивільнення, які імітують взаємодію з клітинною мембраною. Така універсальність дає змогу розглядати ці матеріали як перспективні кандидати для інноваційного застосування в цільових системах доставки ліків і як нанореактори для синтезу наночастинок срібла. Цей огляд підкреслює їхній потенціал у розвитку нанотехнологій і біомедичної інженерії.*

Ключові слова: *піромелітова кислота, піромелітовий діангідрид, поліетиленгліколь, холестерол, поверхнево-активні «геміні»-речовини, солюбілізація, куркумін.*