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Pharmacochemistry

Study of Poly[Oxy-1-Carboxy-2-(3,4-Dihydroxyphenyl) Ethylene] from *Symphytum asperum, S.caucasicum, S.officinale, Anchusa italica* by Circular Dichroism

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(Presented by Academy Member Devi Ugrekhelidze)

ABSTRACT. Comparative study of chirality of two carbon atoms C1 and C2 of poly[oxy-1-carboxy-2-(3,4-dihydroxyphenyl)ethylene] (POCDPE) preparations from different species of Boraginaceae family - *Symphytum asperum, S.caucasicum, S.officinale, Anchusa italica* revealed that they have one and the same absolute configuration in all preparations. It has been established that chiral atoms of POCDPE have either (1*R*,2*R*) or (1*S*,2*S*) configurations but not (1*R*,2*S*) and (1*S*,2R) configurations and consequently the denomination of the polymer is poly[oxy-(1*R*)-1-carboxy-(2*R*)-2-(3,4-dihydroxyphenyl)ethylene] or poly[oxy-(1*S*)-1-carboxy-(2*S*)-2-(3,4-dihydroxyphenyl)ethylene]. *© 2012 Bull. Georg. Natl. Acad. Sci.*

Key words: *poly[3-(3,4-dihydroxyphenyl)glyceric acid], poly[oxy-1-carboxy-2-(3,4-dihydroxyphenyl) ethylene], 3-(3,4-dihydroxyphenyl)glyceric acid, Symphytum asperum, S.caucasicum, S.officinale, Anchusa italica, circular dichroism.*

In previous papers we have reported about the isolation and identification of biologically active poly[3-(3,4-dihydroxyphenyl)glyceric acid] (PDPGA) that is poly[oxy-1-carboxy-2-(3,4-dihydroxyphenyl) ethylene] (POCDPE) from *Symphytum asperum* – POCDPE-SA, *S. caucasicum* – POCDPE-SC, *S. officinale* – POCDPE-SO and *Anchusa italica* – POCDPE-AI, respectively [1-8] (Fig. 1). The repeating unit of POCDPE – 3-(3,4-dihydroxyphenyl)glyceric acid residue contains two asymmetric carbon atoms C1 and C2 (Fig. 2), but we had not yet any information concerning the chirality of these centers.

Besides, the enantiomers of 3-(3,4-dihydroxyphenyl)glyceric acid – the monomer of PDPGA – (+)-(*2R,3S*)-2,3-dihydroxy-3-(3,4-dihydroxyphenyl)-propionic acid [**(***2R,3S***)-**DDPPA**]** (Fig. 3) and (–)-(*2S,3R*)-2,3-dihydroxy-3-(3,4-dihydroxyphenyl)-propionic acid [**(**2*S,*3*R***)-**DDPPA] (Fig. 4) were synthesized from *trans*-caffeic acid [9].

Results and Discussion. Circular dichroism **(**CD**)** spectra of **(**2*R,*3*S***)-**DDPPA and **(**2*S,*3*R***)-**DDPPA are given in Figs. 5 and 6, respectively.

CD spectra show positive Cotton effect at the wavelength 195 nm and negative one at the wave-

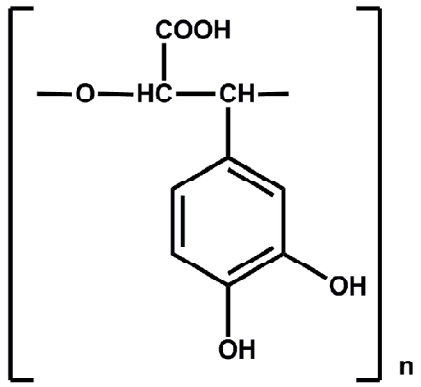

Fig. 1. Poly[oxy-1-carboxy-2-(3,4-dihydroxyphenyl) ethylene] (POCDPE).

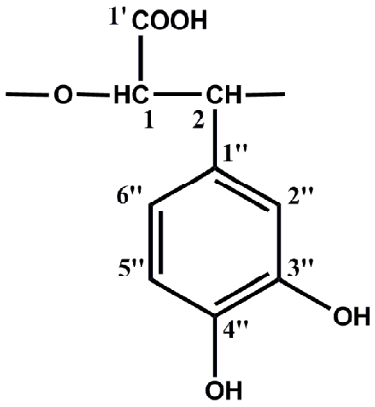

Fig. 2. Repeating unit of POCDPE-SA, POCDPE-SC, POCDPE-SO and POCDPE-AI.

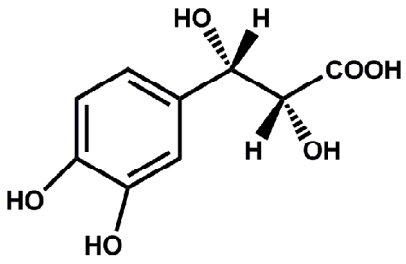

Fig. 3. (+)-(*2R,3S*)-2,3-dihydroxy-3-(3,4-dihydroxyphenyl)-propionic acid [(*2R,3S*)-DDPPA].

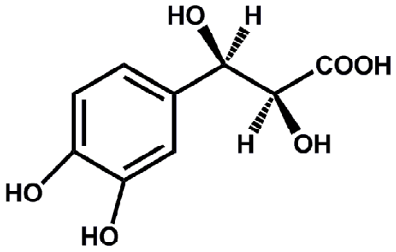

Fig. 4. (–)-(*2S,3R*)-2,3-dihydroxy-3-(3,4-dihydroxyphenyl)-propionic acid [(*2S,3R*)-DDPPA].

lengths 209, 228 and 275 nm for (*2R,3S*)-DDPPA (Fig. 5) and vice versa for (*2S,3R*)-DDPPA (Fig. 6). Thus, Cotton effects in CD spectra of (*2R,3S*)-DDPPA and (*2S,3R*)-DDPPA have opposite profiles (Fig. 7).

The CD spectra of POCDPE-SA, POCDPE-SC, POCDPE-SO and POCDPE-AI have similar profiles and show positive Cotton effects at 194, 214, 280, 286 nm and a negative one at 204, 236 nm (Figs. 8 and 9). These data confirm that two chiral carbon atoms C1 and C2 of the repeating unit of POCDPE-SA, POCDPE-SC, POCDPE-SO and POCDPE-AI (Fig. 2) have one and the same absolute configuration.

Cotton effects in CD spectra of (*2R,3S*)-DDPPA and (*2S,3R*)-DDPPA are shifted about 5-11 nm

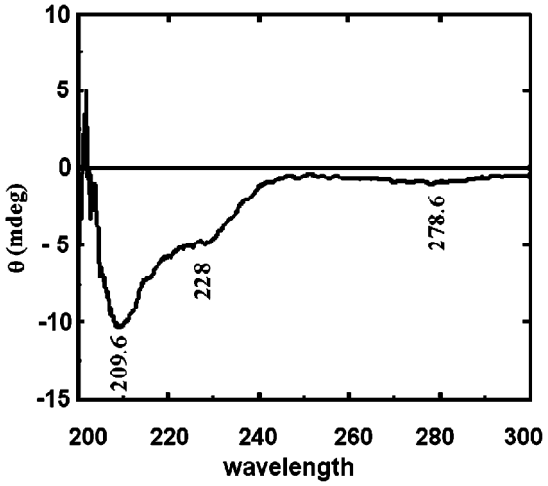

Fig. 5. CD spectrum of (*2R,3S*)-DDPPA.

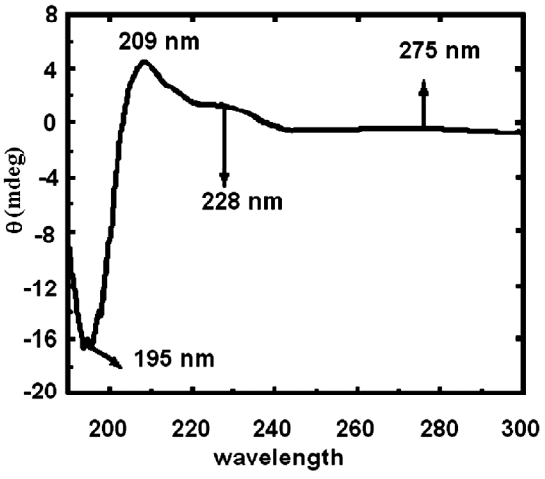

Fig. 6. CD spectrum of (*2S,3R*)-DDPPA.

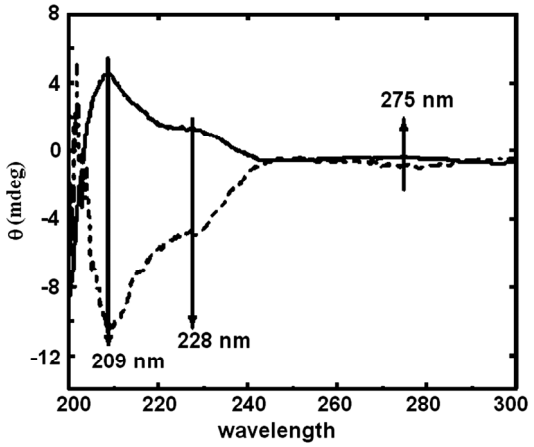

Fig. 7. Comparison of CD spectra of (2*R*,3*S*)-DDPPA (- - -) and (2*S*,3*R*)-DDPPA (——)

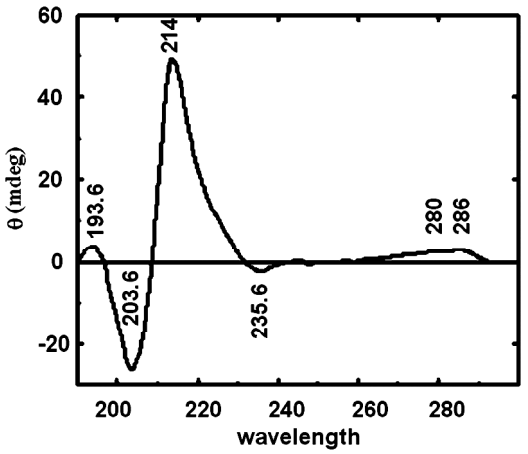

Fig. 8. CD spectrum of POCDPE-SA.

towards lower wavelengths vs Cotton effects in CD spectra of POCDPE-SA, POCDPE-SC, POCDPE-SO and POCDPE-AI.

Cotton effects at 195, 209, 228 and 275 nm in CD spectra of monomers – (2*R*,3*S*)-DDPPA and (2*S*,3*R*)-DDPPA correspond to Cotton effects at the 204, 214, 236 and 286 nm in CD spectra of POCDPE-SA, POCDPE-SC, POCDPE-SO and POCDPE-AI. Besides, as the profiles of CD spectra of polymers (Figs. 8 and 9) do not coincide with CD spectra of (2*R*,3*S*)-DDPPA and (2*S*,3*R*)-DDPPA (Fig. 7) we can exclude (1*R*,2*S*) and (1*S*,2*R*) configurations for chiral atoms C1 and C2 in the repeating units of POCDPE-SA, POCDPE-SC, POCDPE-SO and POCDPE-AI (Fig. 2). Hence, we can suppose that C1 and C2 atoms have either (1*R*,2*R*) or (1*S*,2*S*) configurations and consequently denomination of polymer is poly[oxy-(1*R*)-1-carboxy-(2*R*)-2-(3,4-dihydroxyphenyl)ethylene] or poly[oxy-(1*S*)-1-carboxy-(2*S*)-2-(3,4-dihydroxyphenyl)ethylene].

Establishment of the absolute configuration of these C atoms is a topic for further research.

Materials and Methods. CD spectra were performed on a Jasco J-715 instrument (Jasco Co, Tokyo, Japan) equipped with Peltier temperature control system. For all measurements, 1 mm path length quartz cells, 1 nm bandwidth, 0.2 nm resolution, 1 s response and a scan speed of 50 nm/min for each spectrum were used.

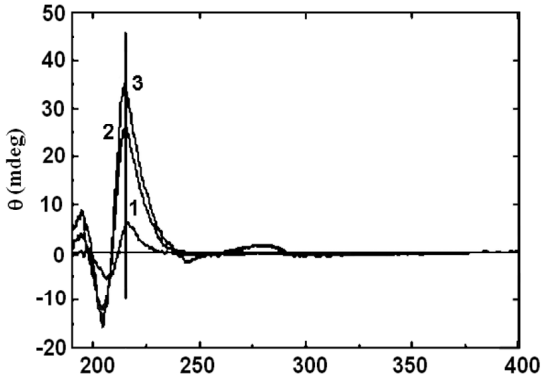

Fig. 9. CD spectra of POCDPE-SC(1), POCDPE-SO(2) and POCDPE-AI(3).

CD spectrum of (2*R*,3*S*)-DDPPA (C = 0.56×10^{-3} M, H_2O): $\Delta\varepsilon_{275} = -1$, $\Delta\varepsilon_{228} = -5$, $\Delta\varepsilon_{209} = -10$, $\Delta\varepsilon_{195} = +5$.

CD spectrum of (2*S*,3*R*)-DDPPA (C = 0.5×10^{-3} M, H_2O): $\Delta\varepsilon_{275} = -0.4$, $\Delta\varepsilon_{228} = +1.8$, $\Delta\varepsilon_{209} = +4.8$, $\Delta\varepsilon_{195} = -16$.

CD spectrum of POCDPE-SA (C = 1.2 mg/10 ml, H_2O): $\Delta\varepsilon_{286} = +3$, $\Delta\varepsilon_{236} = -2$, $\Delta\varepsilon_{214} = +50$, $\Delta\varepsilon_{204} = -28$, $\Delta\varepsilon_{194} = +4$.

ფარმაკოქიმია

Symphytum asperum-ის, *S.caucasicum*-ის, *S.officinale*-ს, *Anchusa italica*-ს პოლი[ოქსი-1-კარბოქსი-2-(3,4-დიჰიდროქსიფენილ)ეთილენის] შესწავლა წრიული დიქროიზმის მეთოდით

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Boraginaceae-ს ოჯახის სხვადასხვა სახეობების (*Symphytum asperum, S. caucasicum, S.officinale* და *Anchusa italica)* პოლი[ოქსი-1-კარბოქსი-2-(3,4-დიჰიდროქსიფენილ)ეთილენის] (პოკდფე) პრეპარატების ორი ნახშირბად ატომის C1 და C2 ქირალობის შედარებითმა შესწავლამ აჩვენა, რომ ყველა პრეპარატში მათ აქვთ ერთი და იგივე აბსოლუტური კონფიგურაცია. დადგენილია, რომ პოკდფე-ს ქირალურ ატომებს აქვთ ან (1R,2R) ან (1S,2S) კონფიგურაციები, მაგრამ არა (1R,2S) და (1S,2R) კონფიგურაციები და აქედან გამომდინარე პოლიმერის სახელწოდება შეიძლება იყოს პოლი[ოქსი-(1R)-1-კარბოქსი-(2R)-2-(3,4-დიჰიდროქსიფენილ)ეთილენი] ან პოლი[ოქსი-(1S)-1-კარბოქსი-(2S)-2-(3,4-დიჰიდროქსიფენილ)ეთილენი].

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