

Molecular effects of silymarin flavonolignans: Chirality matters

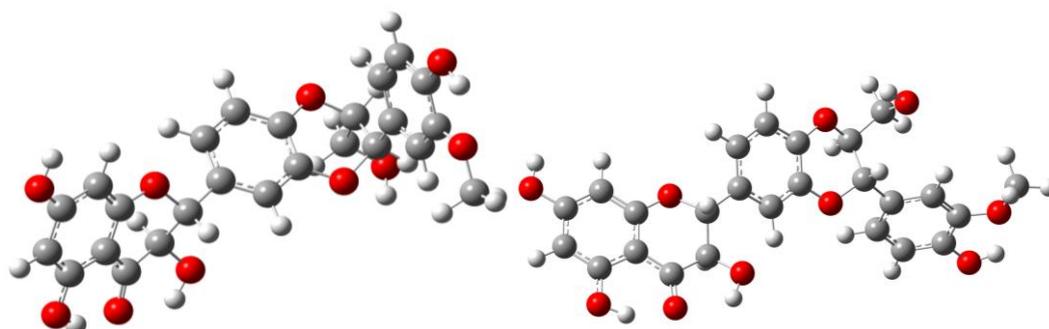
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Silymarin (extract from the milk thistle fruit - *Silybum marianum*) has been traditionally used in various medicinal applications since ancient times. A number of controversies often arise, mainly due to the non-standard composition of this phytopreparation, the use of various undefined mixtures, the misattribution of silymarin vs. silybin, and the failure to consider the chemistry of the individual components of silymarin [1]. A major component of silymarin is the flavonolignan silybin [2] and its congeners isosilybin, silychristin, silydianin, and the dehydroderivative 2,3-dehydrosilybin. All these compounds (except silydianin) occur in nature as two diastereomers [3]. Since their isolation in 1959, silybin and other flavonolignans have attracted increasing interest, leading to the publication of ca 500 research articles per year (in the last 10 years).

We will show that the specific activities of the respective diastereomers of flavonolignans and also of the enantiomers of their 2,3-dehydro derivatives differ significantly in the 3D anisotropic systems (typically biological systems). *In vivo*, silymarin flavonolignans do not act as redox antioxidants - silybin is even a very poor antioxidant - but they play a role as specific ligands of biological targets following the "lock-and-key" concept. This also allows the separation of the respective diastereomers by enzymatic methods [4].

Estrogenic, antidiabetic, anticancer, antiviral, and antiparasitic effects will be demonstrated in optically pure flavonolignans. Potential applications of pure flavonolignans have also been shown in cardiovascular and neurological diseases. Inhibition of drug metabolizing enzymes and modulation of multidrug resistance by these compounds are discussed in detail [5]. The future of "silymarin applications" lies in the use of optically pure components that can be directly applied or used as valuable lead structures, and in the exploration of their true molecular effects.



Silybin A

Silybin B

Acknowledgements: This study was supported by a grant from the Czech Science Foundation No. 21-01799S.

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