

Isolation of 2-arylbenzofurans and stilbenes with potential anti-inflammatory activity and their metabolism in model of colon microbiota

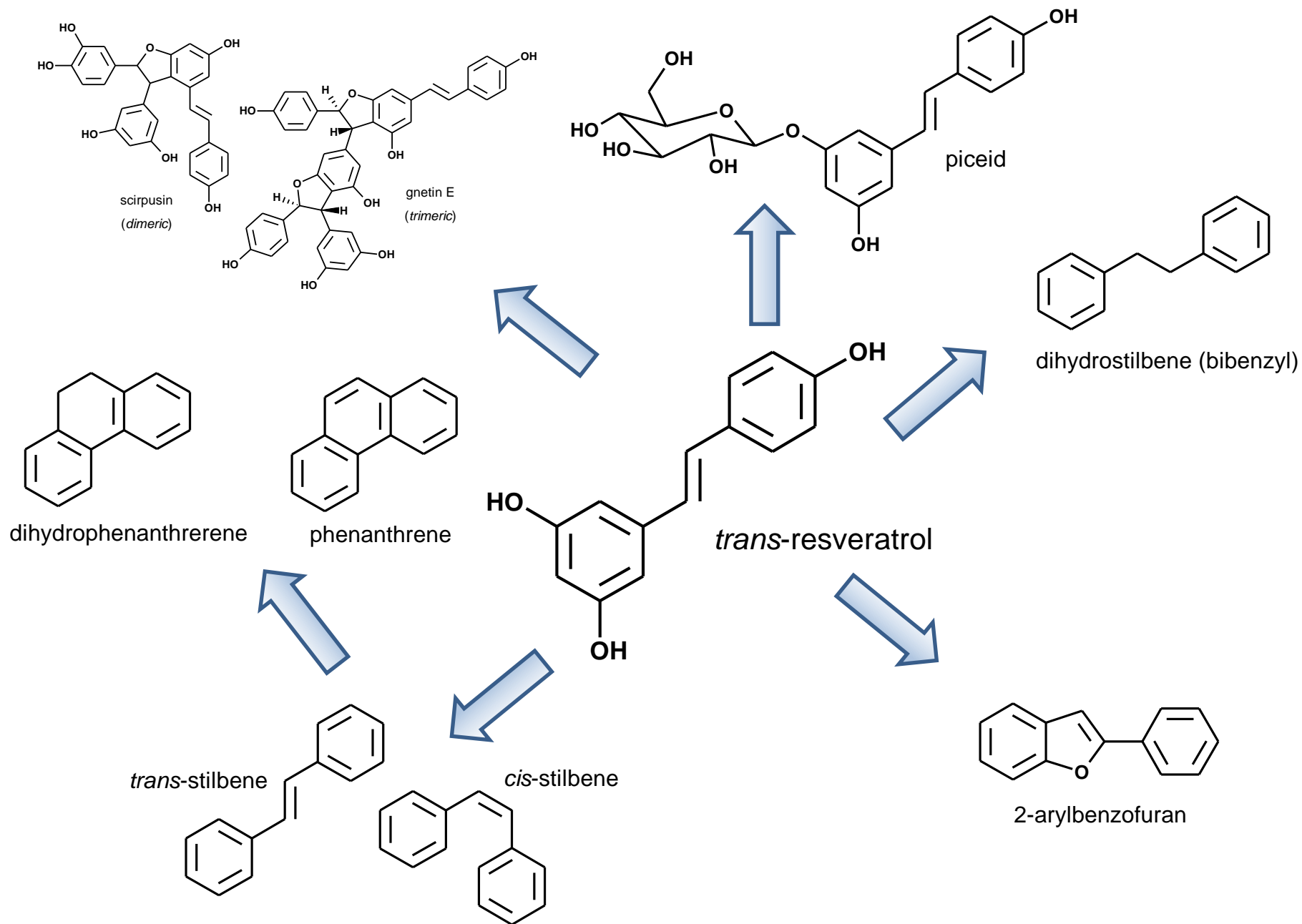


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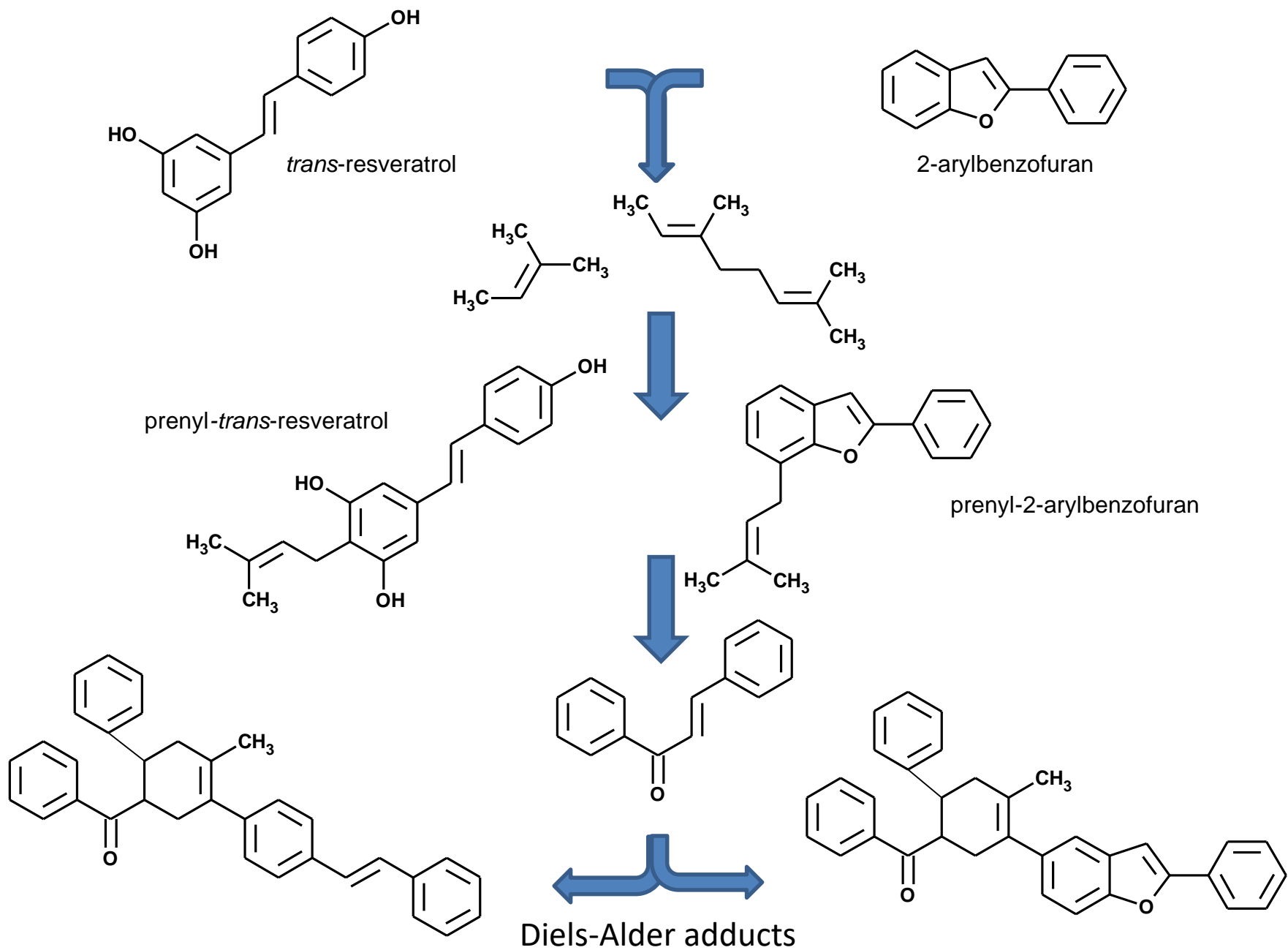
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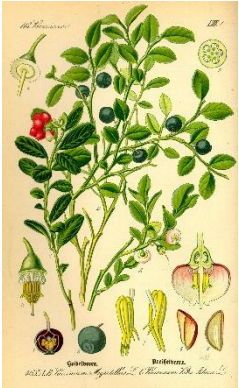
Stilbenoids – plant secondary metabolites



Prenylated stilbenoids



Biologic activity and sources of stilbenoids



Vaccinium spp.



Vitis spp.



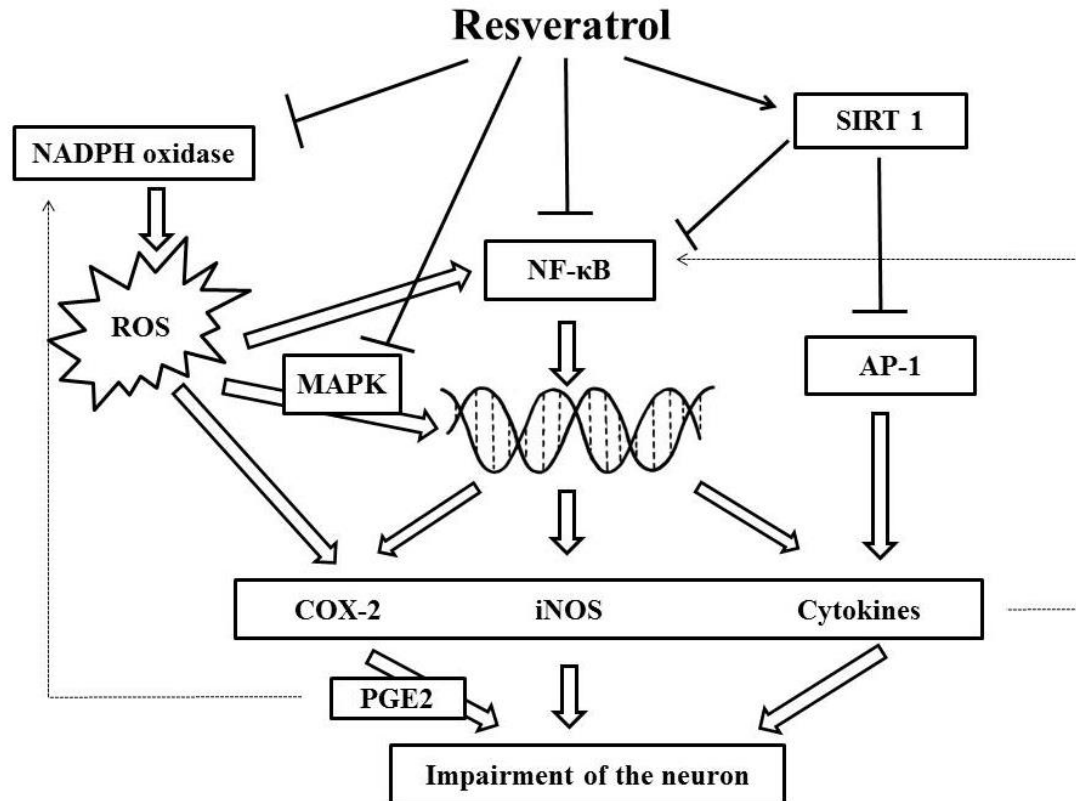
Arachis hypogaea

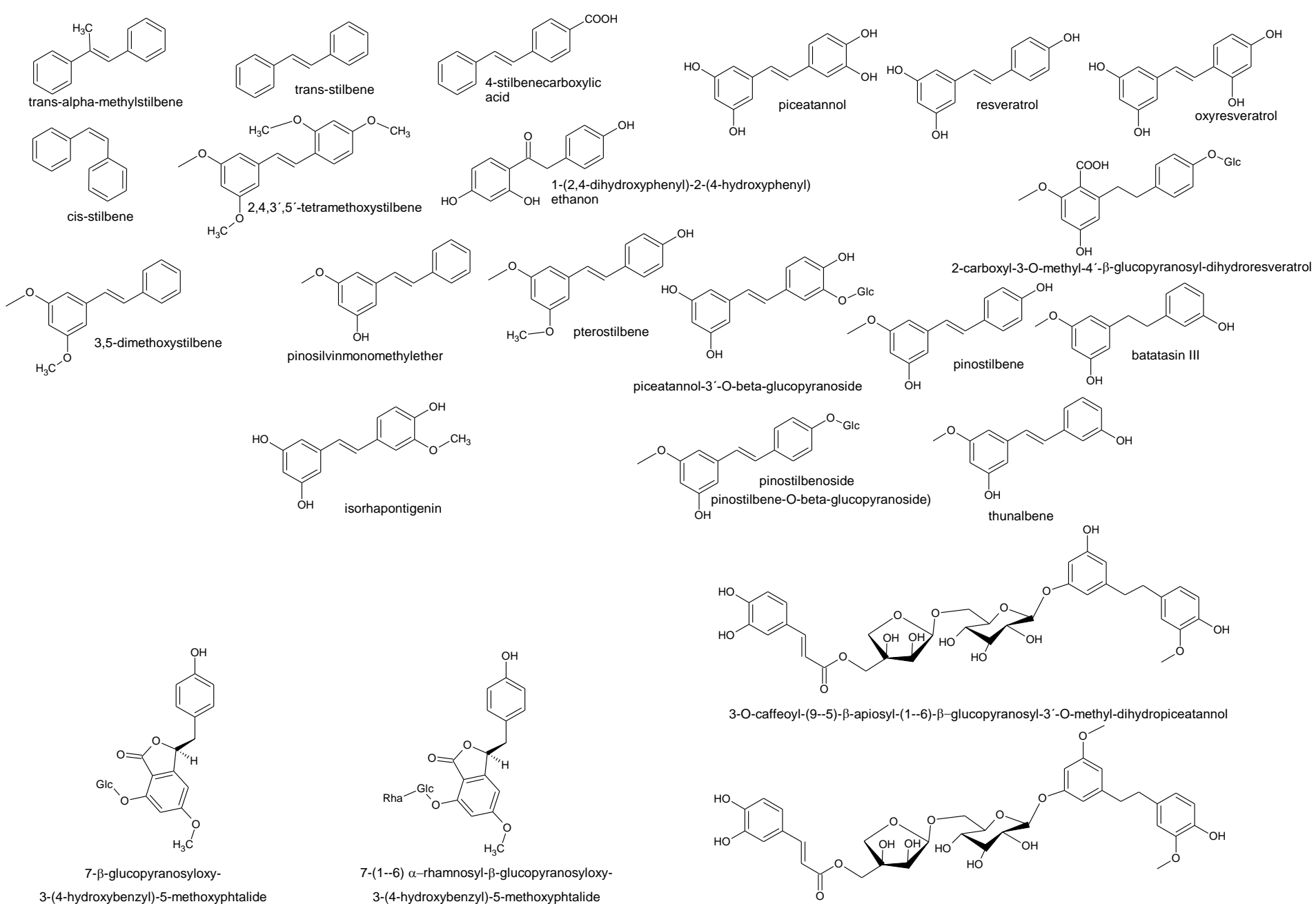


Morus spp.

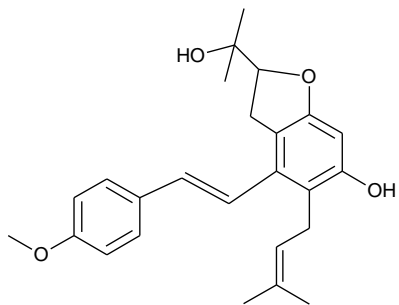


Artocarpus spp.

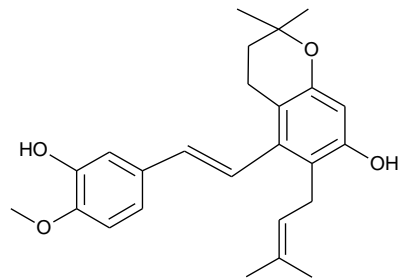




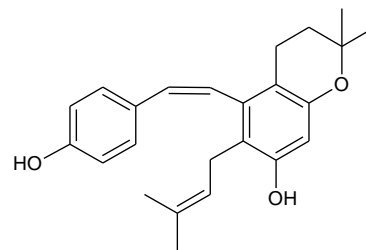
23 stilbene and dihydrostilbene derivatives



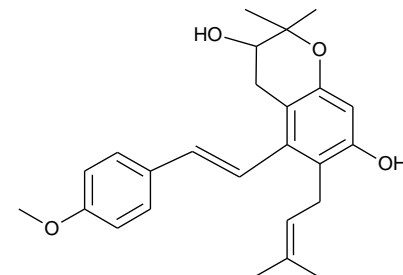
N-MS-27-B4



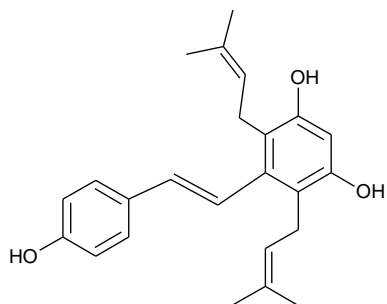
N-MS-70-B1



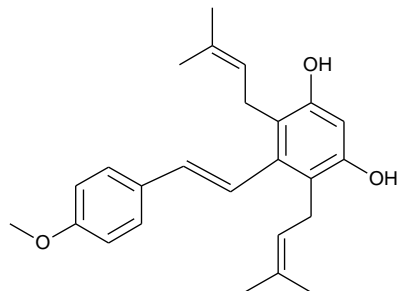
N-NS-74-F11



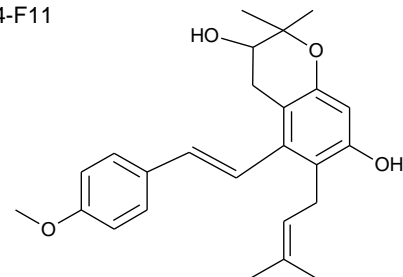
N-MS-22-B2



N-MS-30-F2



N-MS-12F4C2



N-MS-13-F5

7 prenylated stilbenes



Thanks to Pavel Bobál' (UVPS Brno) for effort on synthesis of stilbenoid derivatives.

Sebastian Granica (Medical University of Warsaw, Poland) - *Tragopogon* stilbenoids

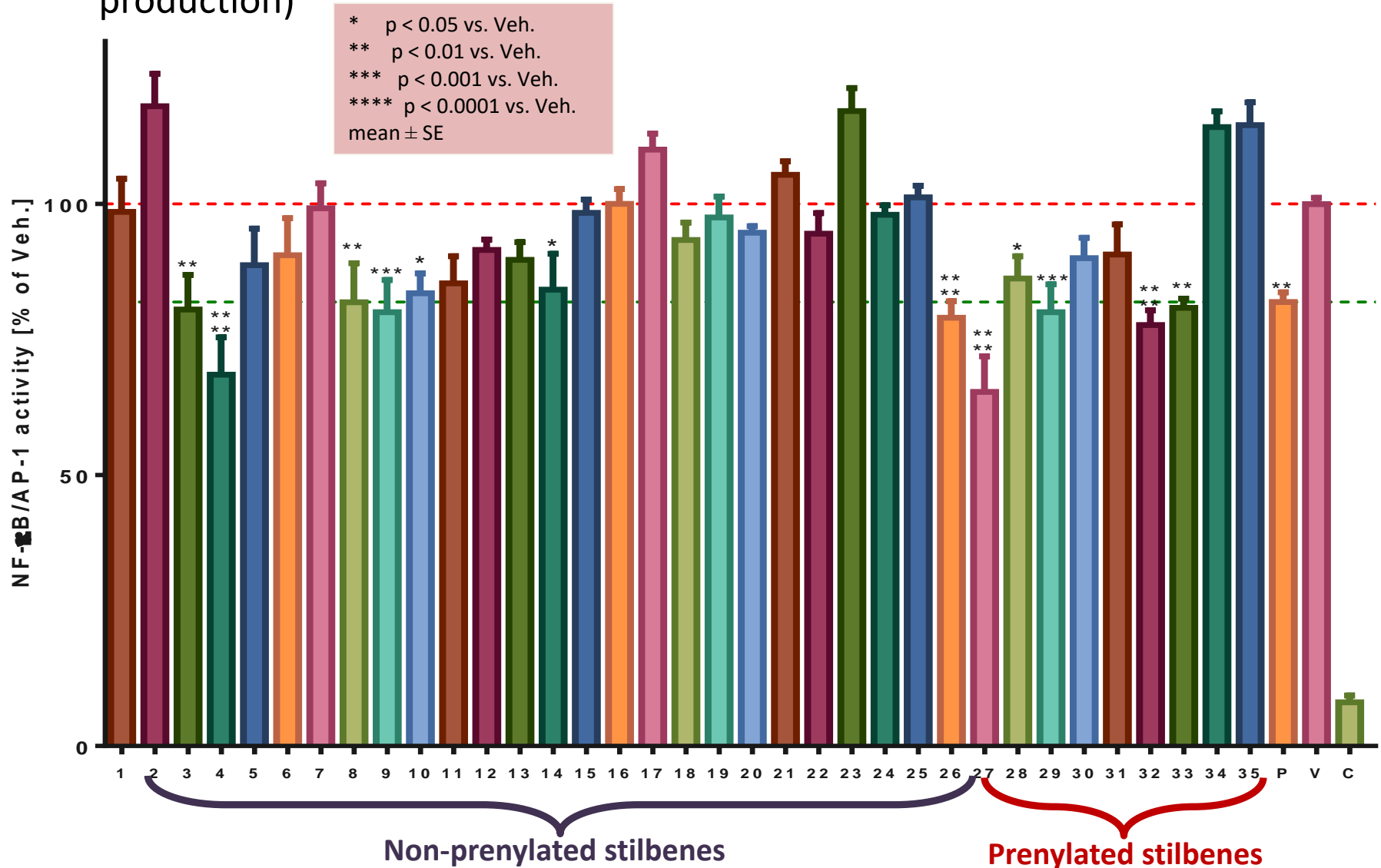
Vilailak Prachyawarakorn (Chulabhorn Graduate Institute, Thailand) prenylated stilbenes from *Macaranga*.

Gang Ren (Research Center of Natural Resources of Chinese Medicinal Materials and Ethnic Medicine, Jiangxi University of Traditional Chinese Medicine, China) prenylated compounds from *Artocarpus heterophyllus*.

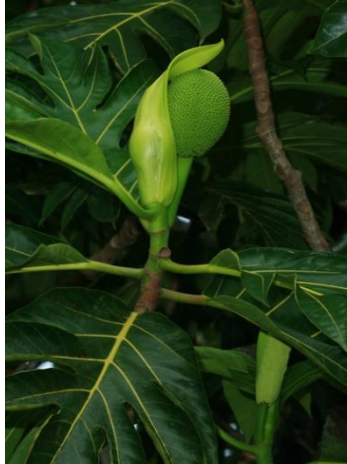
Synthetic prenylated stilbenoids
Commercial sources
Cooperation

Inhibition of NF-κB/AP-1

- THP1-XBlue™-MD2-CD14 cell line
- NF-κB/AP-1 detection after 24 h (using QUANTI-Blue™ Assay to detect SEAP production)



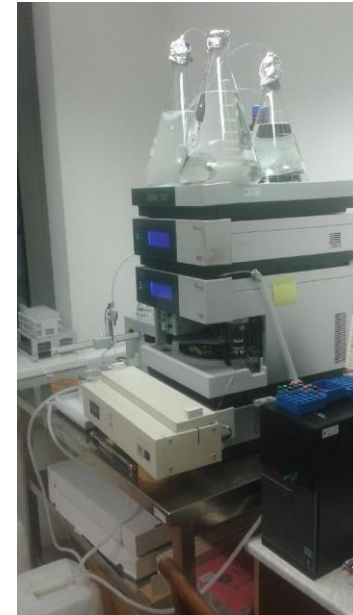
Isolation and identification of stilbenoids



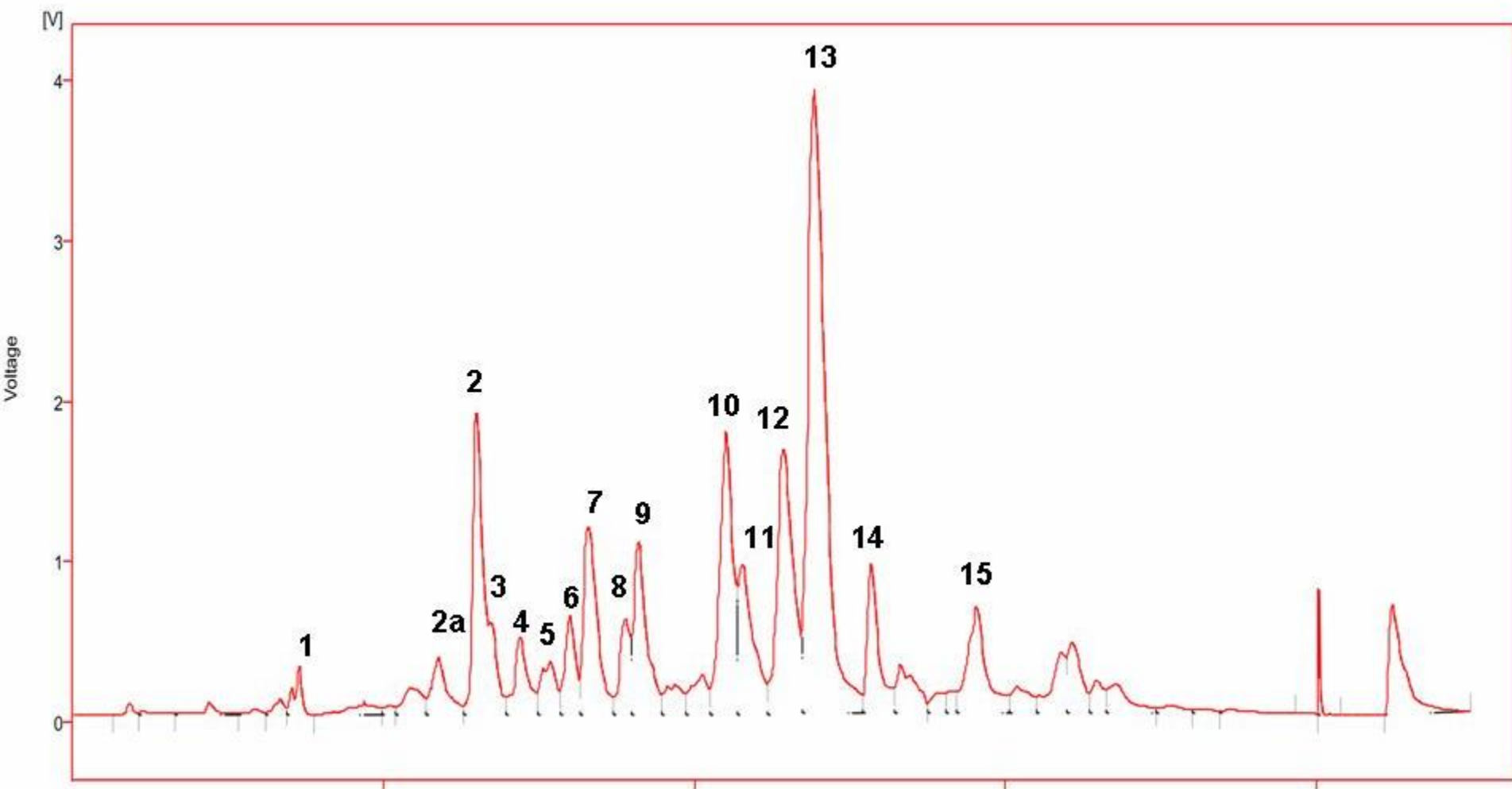
Artocarpus altilis
wood

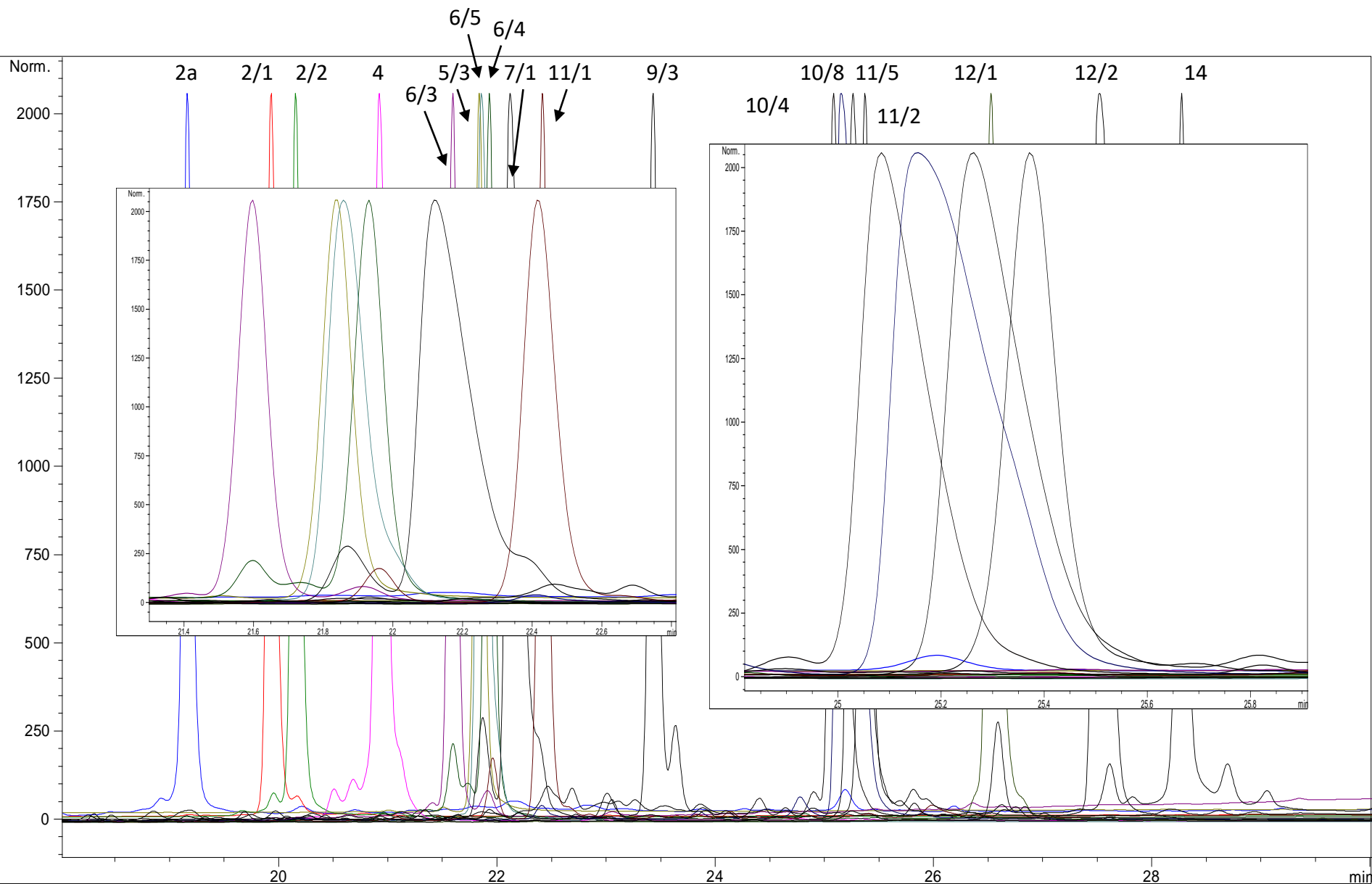


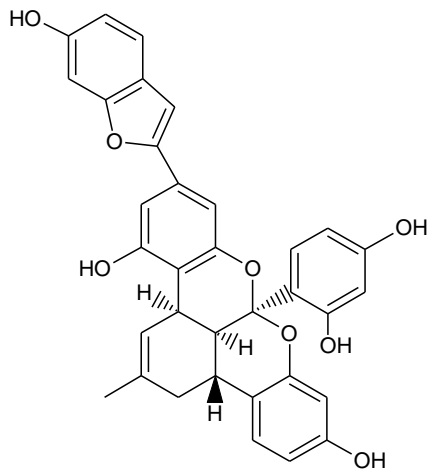
Morus alba
root bark



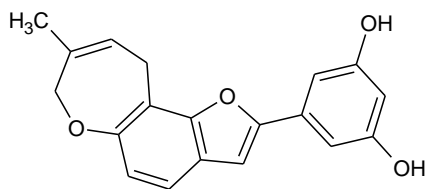
Example of preparativeHPLC analysis of *M. nigra* chloroform portion of total extract.



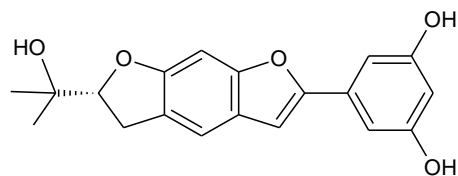




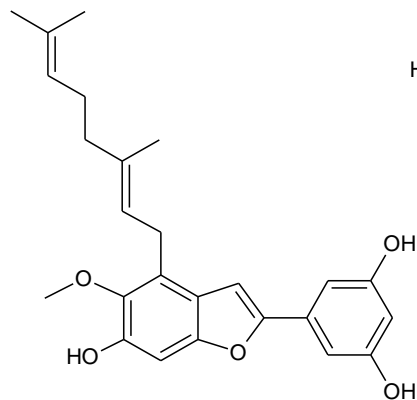
Mulberrofuran G (albanol A)



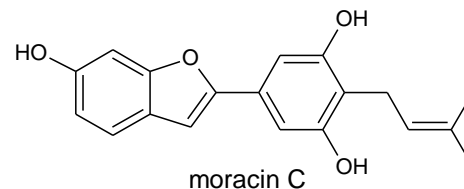
mulberrofuran B



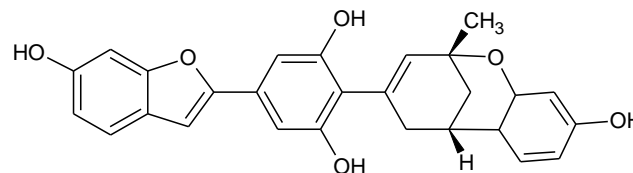
moracin O



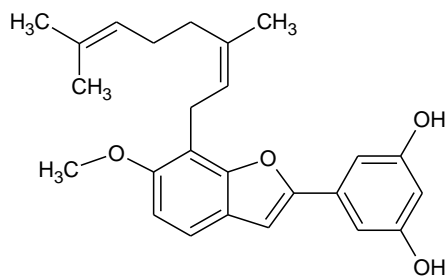
mulberrofuran Y



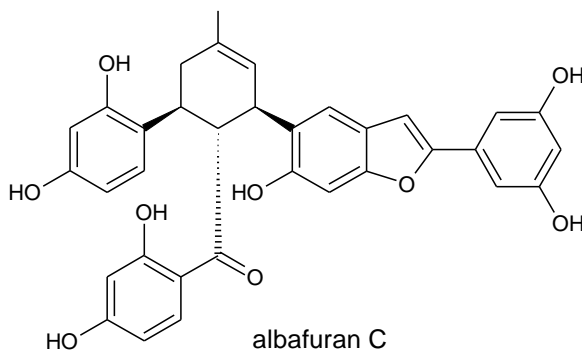
moracin C



mulberrofuran H

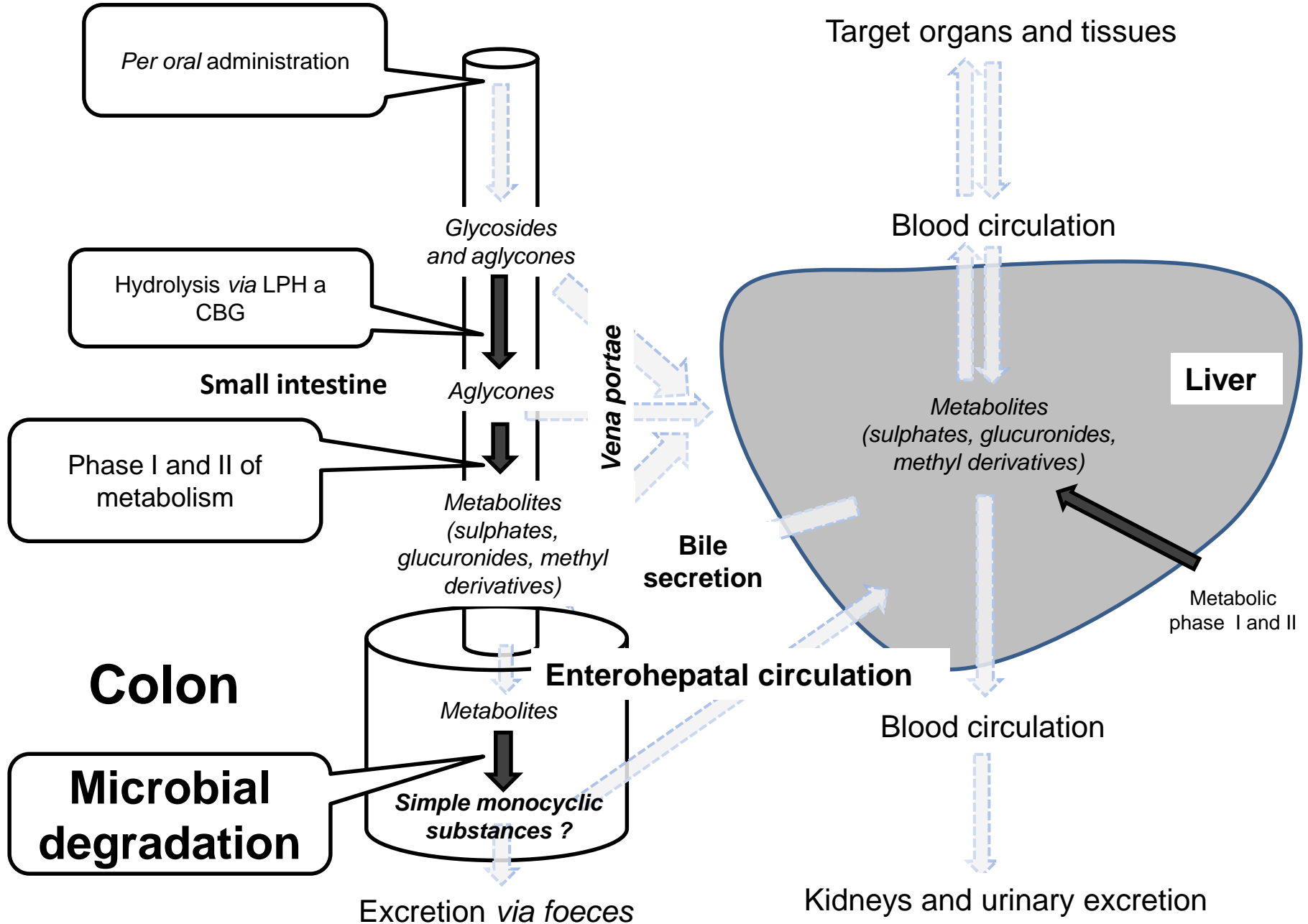


mulberrofuran L



albafulan C

Metabolism of stilbenoids



Metabolisation of stilbenoids in model of colon microbiota

**Simulation
of colonic
microbiota**

Donor with non-phenolics diet
Feces mixed and dispersed in cultivation
medium
Inoculation with stilbenoids
Inoculation with ^{13}C -resveratrol

Fermentation and sampling in 0, 2, 4, 8, 24
and 48 hours

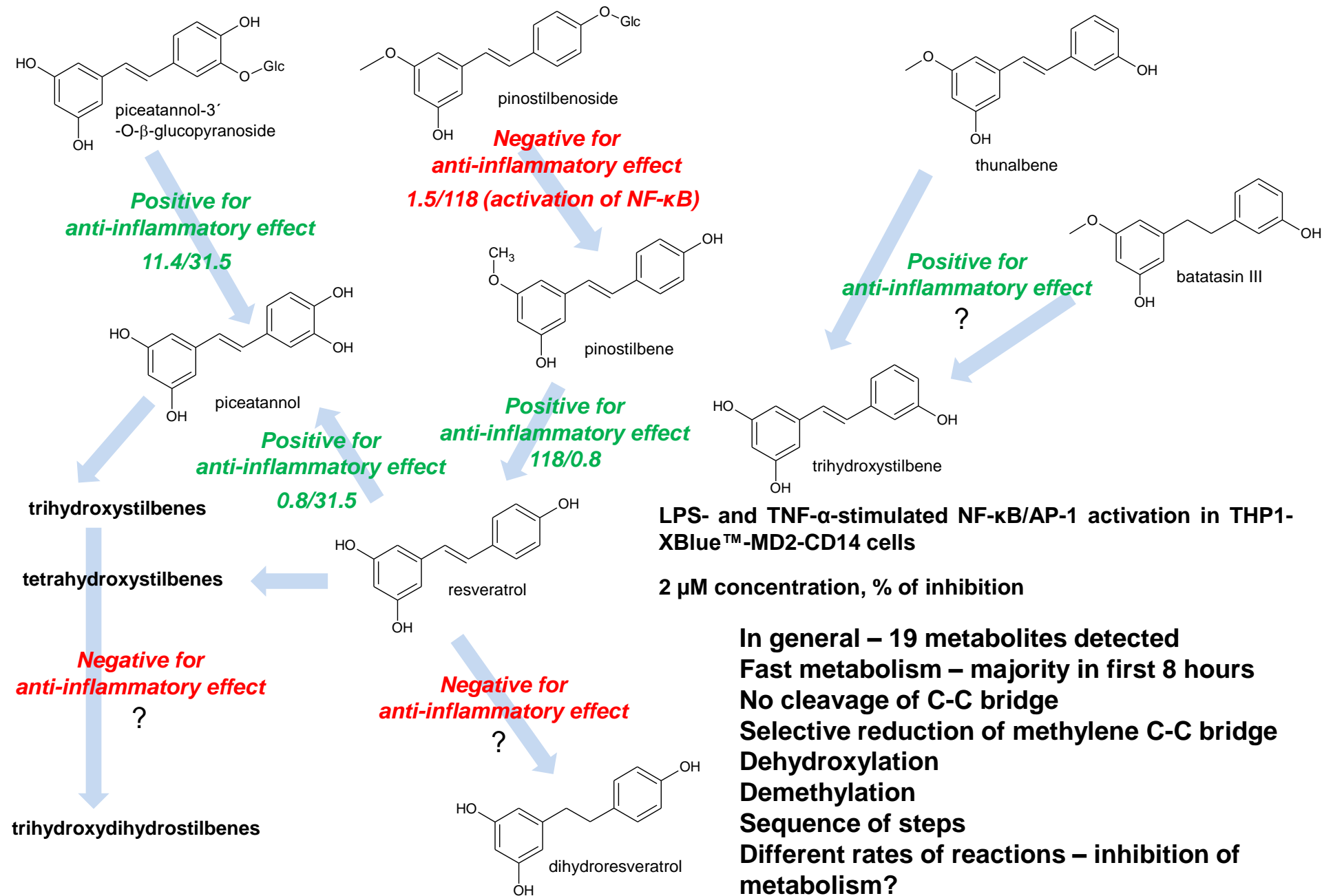


Sample purification and pre-concentration

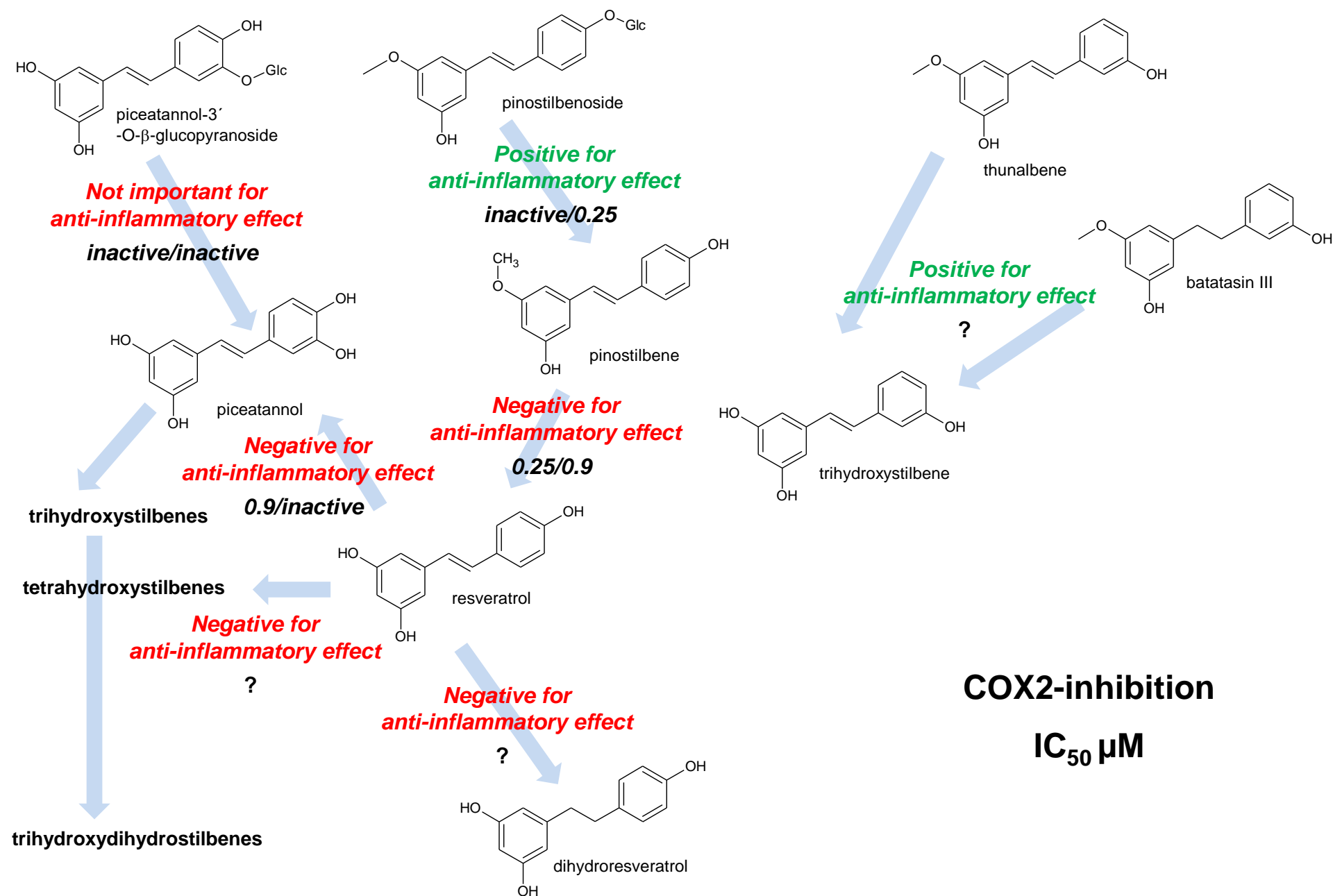


LC-MS analysis

Metabolisation of stilbenoids in model of colon microbiota



Metabolisation of stilbenoids in model of colon microbiota



Conclusions

- Isolation of several prenylated stilbenoids with potential anti-inflammatory effect
- Successfully established method for colonic microbiota metabolisation
 - Testing of non-prenylated stilbenoids – common metabolisation, no monocyclic metabolites detected
 - No metabolites identified for prenylated 2-arylbenzofurans

Perspectives

- To observe metabolism in system of co-cultivated Caco-2 and HT cells
- To continue the isolation of further prenylated compounds
- To identify metabolites of prenylated stilbenoids and 2-arylbenzofurans
- Scale up the fermentation process to obtain sufficient amounts of metabolites for anti-inflammatory activity testing
- To prepare commercially non-available metabolites for testing of anti-inflammatory effect

Thanks for attention.

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Thanks to Přemysl Landa (Institute of Experimental Botany, Academy of Science Czech Republic) for COX inhibition analysis.

Thanks to Pavel Bobál' (UVPS Brno) for effort on synthesis of stilbenoid derivatives.

Thanks to Sebastian Granica (Medical University of Warsaw, Poland) for providing us with *Tragopogon* stilbenoids.

Thanks to Vilailak Prachyawarakorn (Chulabhorn Graduate Institute, Thailand) for providing us with prenylated stilbenes from *Macaranga*.

Thanks to Gang Ren (Research Center of Natural Resources of Chinese Medicinal Materials and Ethnic Medicine, Jiangxi University of Traditional Chinese Medicine, China)) for providing us with prenylated compounds from *Artocarpus heterophyllus*.

