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Polyphenolic compounds from *Ampelopsis japonica* inhibit Wnt signaling

Key words: Wnt signaling pathway, Ampelopsis japonica

Triple negative breast cancer (TNBC) is the most aggressive breast cancer type. The majority of TNBC cases are associated with improper activation of the intracellular Wnt signaling pathway. Targeted hormonal and anti-HER₂ therapies is ineffective when treating TNBC. Thus, the search for selective modulators of the Wnt pathway, including metabolites from natural sources, is one of the most important tasks in the field of pharmacological research aimed at treating cancer.

One of the plants producing metabolites that can inhibit Wnt signaling is a Far Eastern endemic plant *Ampelopsis japonica*. Its water-alcohol extract has been shown to selectively suppress Wnt activity in TNBC cells. In order to isolate the active compounds we applied this extract to a polyamide column and subsequently eluted polyphenolic compounds with hexane (fraction A), chlorophorm (fraction B), chlorophorm:ethanol 10:1 (fraction C), ethanol (fraction D) and water (fraction E). All the fractions were tested for the ability to effectively suppress Wnt signaling in HTB-19-TOPFLASH cells using the double luciferase analysis technique. Fractions C and D showed the most significant activity. Treatment of cells by this fractions has reduced the Wnt-activated luminescence to the background level. The ethanol fraction was then subsequently applied to a Toyaperl HW-50 column and to a C-18 column. Fractions 4, 11 and 14 significantly inhibited Wnt signaling (Fig. 1) at a concentration of 5 ng per 1 mkl of culture medium. According to LC-ESI-MS data these fractions contained individual compounds **1**, **2** and **3** respectively. Their molecular masses and maxima in UV spectra are shown in Table 1.

Table 1 – LC-MS data for compounds 1-3.

Compound	UV-spectrum	[M+H] ⁺	[M-H] ⁻
1	280	291	289
2	274	-	331
3	274	-	331

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This study was supported by the Russian Foundation for Basic Research (grant 18-34-00502 mol_a).

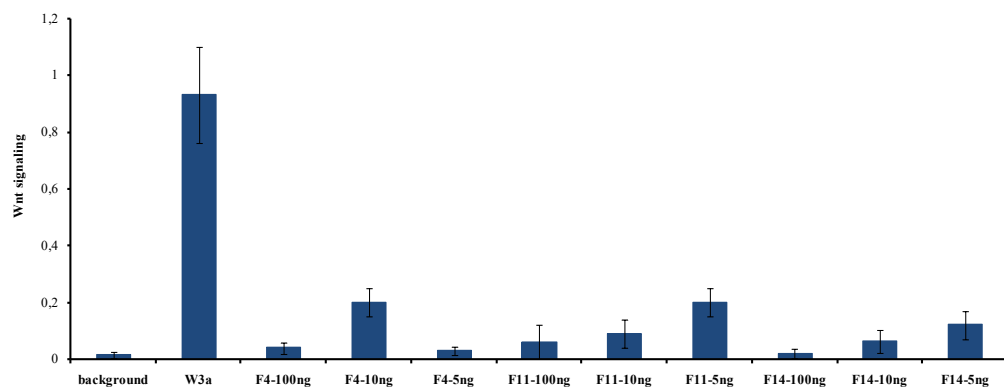


Fig. 1 – Wnt suppressing activity of polyphenolic compounds from *Ampelopsis japonica* (background – background luciferase activity, W3a – the activation of luminescence by Wnt3a protein).