Berberine inhibits interleukin-5-induced Stat5 activation for proliferation and survival of pro-B Y16 cells

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Berberine, an isoquinoline alkaloid, is known to have several pharmacological properties such as anti-inflammation and anti-cancer. Interleukin (IL)-5 is a Th_2 cytokine involved in the allergic inflammation. In this study, we investigated the effect of berberine on IL-5-dependent growth or survival of pro-B Y16 cells. Berberine inhibited IL-5-dependent proliferation of Y16 cells with an IC_{50} value of 13 μM. This effect of berberine was associated with a cell cycle arrest at G1 phase, which was coincided with down-regulation of cyclins D3 and E1 as well as cyclin-dependent kinase (Cdk)-2, but also up-regulation of Cdk inhibitory proteins of p21/Cip1 and p27/Kip1. Furthermore, berberine inhibited IL-5-induced survival of Y16 cells with an IC_{50} value of 18 μM. This effect of berberine was mediated though apoptosis, documented by DNA fragmentation and plasma membrane disruption, which was substantially correlated to its down-regulatory effect on anti-apoptotic proteins Bcl-2 and Mcl-1. Since IL-5 mediates its cellular response through Stat5, a transcription factor for cell proliferation and survival, we demonstrated that berberine could inhibit IL-5-induced Stat5 activation in the Y16 cells and down-regulate IL-5-induced expression of c-myc, a target gene of Stat5. Taken together, berberine inhibited IL-5-dependent proliferation of Y16 cells through G1 arrest and also decreased IL-5-induced survival of the cells through apoptosis, which was primarily attributable to its effect on Stat5 activation.

Key words: Berberine, IL-5, Stat5, Cell cycle, Apoptosis, Pro-B cells.