

## A SYSTEMATIC REVIEW OF THE UTERINE RELAXANT EFFECT OF HERBAL SOURCES

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Preterm birth is a worldwide tragedy with a high incidence. Several medications, are used to inhibit acute preterm labor; but tocolysis by these drugs do not extend pregnancy beyond 1-2 days. So new medications should be discovered for the treatment of preterm labor. For this purpose we reviewed all studies in which plant extracts or their effective materials inhibit the uterine contractions. All electronic databases were searched up to 1<sup>st</sup> February 2012 with the most relevant keywords. Studies related to the relaxant effect of plant extracts or their effective materials on the human or animal myometrium both *in vivo* and *in vitro* were included. Of initial search, 259 records were reviewed and finally, 72 were included.

About the mechanism of these plant extracts or their effective materials we found that the nitric oxide pathway, unlike human myometrium, dose not play an important role in relaxation of pregnant and non-pregnant rat myometrium, but it probably acts on laboring rat myometrium. Another issue is about the store operated calcium entry (SOCE), a voltage independent calcium entry pathway, which is upregulated in late pregnant and active laboring rat myometrium and causes an increase in basal tone in these tissues, which is nifedipine resistant. In this review, agents which blocked agonist-induced myometrium contractions in a calcium free solution, probably acted via blocking the SOCE. SOCE can block by cyclic nucleotides.  $\beta$ -agonists and phosphodiesterase(PDE) inhibitors can increase the cyclic nucleotides, but unlike  $\beta$ -agonists which are desensitizing at the end of the pregnancy, PDE inhibitors can completely relax the pregnant myometrium. Studies have shown that some of the effective materials that were reviwed in this study(osthole, Naringenin, Kaempferol and quercetin) are PDE inhibitors.

**Conclusion:**It seems that laboring uterus responsiveness to different tocolytics vary from non-laboring uterus, so further studies should work on the pharmacology of the laboring uterus and evaluated the effect of these PDE inhibitor materials on blocking the SOCE, in human laboring myometrial cells and also determine the structure activity relationship of these tocolytic compounds.

