Medicinal plants and reproduction

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Medicines (agents and drugs) obtained from plants have been processed for thousands of years and they are often considered as herbal medicines, natural medicines, complement medicines, alternative medicines, or traditional medicines.[1] Since these plants contain mixed and complex components, many of them need a series of processes such as heating, drying, boiling, gridding, shading, compressing, and other physic procedures; and of most importance, the chemical procedures are needed for titration or extraction of a variety of biologically active substances isolated from plants, under the assistance of different types of solvents such as ethanolic, oil, dimethyl sulfoxide, hydroalcohol, or aqueous solution. The preparation of these complicated compounds should follow the guidance of the traditional healers. Fertility is possibly the most important capability contained within living cells or species, contributing to searching for the most efficacious way to enhance or promote fertility for all living things.[2]

Medicinal plants for birth control, either enhancing or blocking purposes, have long been incorporated into medical practice worldwide.[2–8] Active antifertility agents are mainly focused throughout the world, because human population has reached to a critical point, resulting in poverty and deficiency of food and water. However, the synthetic contraceptive agents, although it is highly effective, often result in severe adverse events, and even morbidity and mortality. Therefore, the relatively cheap, widely available, accepted, effective, and natural antifertility compounds obtained from medicinal plants, as shown earlier, are important for healthcare programmes.[2–5] In contrast, the certain areas and countries, including Taiwan, because of few births, showed the decreased size of population and deficiency of man-power, where subfertility or infertility have become the urgent national safety issue, contributing to the eagerly looking for assistance or enhancement of agents to achieve parenthood in couples.[6–8] As shown earlier, although assisted reproductive techniques (ARTs) are powerful and very effective, many couples have faced strong challenges and disappointing or negative experience of ARTs, based on unfriendly therapeutic course and high possibility of adverse events.[9–11]

Nutrition, essential trace elements, and certain "nature or concentrated compounds" are reported to have an ability for improving fertility.[12] In contrast, organic elements and certain "natural or medicinal plants" are reported to be antifertile or abortifacient.[2–5,13] Unfortunately, the mechanisms of these "fertility-enhancing" or "fertility-impairing" compounds are still uncertain. In the March issue of the *Journal of the Chinese Medical Association*, in Drs. Poli and Challa's article, an animal study was conducted to evaluate the antifertility efficacy of eugenol (EUG) and *Ocimum sanctum* (OS) Linn. (Tulsi) leaf extract in female albino rats.[14] The authors found that combination of EUG and Tulsi leaf extract significantly increased the serum levels of estradiol and progesterone leading to decreased frequency of ovulation and subsequent impairment of fertility.[14] The current study is interesting and worthy of discussion.

First, the authors have completed a relatively difficult work, including recording each phase of cycles and hormone profiles. In addition, the authors performed the tissue evaluation by biochemical assay. The authors found that all phases (proestrus, estrus, metestrus, diestrus) of cycle treated with EUG and Tulsi showed variable prolongation compared with those in controls, contributing to prolonging whole duration of cycle.[14] On the basis of the above finding, it is reasonable to suppose the delayed ovulation and agree the authors' conclusion: decreased frequency of ovulation. However, is it real? Furthermore, did it result in the impairment of fertility? In fact, the difference of the current study is only one day (25%, 1/4): 4 days (107 hours) versus 5 days (125 hours).[14] If we consider the normal menstrual cycle of human beings ranging from 21 days to 35 days (mean 28 days), the difference between the long period and short period/mean period) was also 25%, 7/28 and 67%, 14/21, respectively. No evidence supported that pregnancy rate was significantly lower in women with 35-day cycle and higher in those with 21-day cycle.

Second, hormone profile is a very important issue in the success of pregnancy, because abnormal hormone profile not only influences the ovulation but also involves implantation.[15] We totally agree with the deterioration or impairment of ovulation and implantation occurs when estradiol and progesterone concentrations were abnormal. Both high and low concentrations of estradiol and progesterone affect ovulation, implantation, and pregnancy rate. In addition, synchronous and orchestra section of either estradiol or progesterone is a critical step for successful

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pregnancy. However, the authors did not clearly demonstrate the relationship between hormone profile and cycle. It is not clearly why the combination of EUG and Tulsi will increase both concentrations of estradiol and progesterone. It is also very interesting to find testosterone levels were significantly decreased in female mice treated with EUG and Tulsi. Did this combination directly activate or stimulate one of the key enzymes synthesizing estrogen from androgen: aromatase? In addition, since the process of synthesis of estrogen from androgen occurs in granulosa cells within the follicle of the ovary, if the immunohistochemical staining (histological features available) or enzyme activity of aromatase could be done in the current study to show the hyperplasia of granulosa cells or high expression of aromatase, this hypothesis could be tested. Finally, the test for reproductive performance should be finished by live births (the size of litters and the total number of pups). Without further experiments, it might be overstated about the antifertility effect of the combination of EUG and Tulsi.

Since the topic of the current article is interesting, we hope to see more studies to discuss this topic—medicinal plants for fertility—and help us to search for the cheap, widely available, accepted, effective, and natural fertility-enhancing or fertility-impairing compounds obtained from medicinal plants.

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