



如何撰寫論文的 緒論章節

慈濟醫學院生理學科
李文森客座教授

wslee@mail.tcu.edu.tw

ext. 12711

Introduction的內容

- 研究主題的重要性
- 過去的相關研究發現
- 簡述本研究發現

緒論一開始要明確指出你所提出
的問題為何值得研究

該領域所關切的問題

過去研究的結果及所遇到的瓶頸

為何進行本研究

Magnolol Suppresses Proliferation of Cultured Human Colon and Liver Cancer Cells by Inhibiting DNA Synthesis and Activating Apoptosis

The occurrence of gastrointestinal cancers has increased strikingly during the last decade. For instance, colorectal cancer is the second leading cause of cancer mortality in Western societies and one of the most common malignancies worldwide [Chinery et al., 1997]. Liver cancer is one of the most prevalent and deadly cancers in the world, causing almost one million deaths annually [Akriviadis et al., 1998]. Although intensive research during the past few years has led to considerable improvement in the treatment and diagnosis at an early stage, for the patient at this time, the prognosis is still not good. Therefore, experimental and clinical investigators continue to search for new therapeutic strategies. One approach, as pursued in this study, seeks to identify medicinal agents capable of retarding the cell cycle and/or activating the cellular apoptotic response in the cancerous cells.

Magnolol, a hydroxylated biphenyl compound isolated from *Magnolia officinalis*, is a widely used Chinese herbal medicine known as Hou p'u. Traditionally, it has been employed to treat such diverse ailments as headache, fever, etc. [Fujita et al., 1973]. Studies using purified magnolol have shown that it can function to scavenge hydroxyl radicals [Haraguchi et al., 1997], inhibit neutrophil adhesion [Shen et al., 1998], suppress the inflammatory response [Wangetal., 1992], inhibit platelet aggregation [Ko et al., 1989], and may also exhibit certain antimicrobial actions [Chang et al., 1998]. **Of particular interest for the present study is the magnolol-induced suppression of a cutaneous papilloma**, which was induced in mice treated with dimethylbenz[a]anthracene (DMBA) and 12-O-tetradecanoylphorbol-13-acetate (TPA) [Konoshima et al., 1991]. Our study was done to investigate any anti-cancer effects of magnolol on human hepatoma and colon carcinoma cells.

Progesterone inhibits arterial smooth muscle cell proliferation

Cardiovascular disease, the principal cause of death in the developed world, affect men far more frequently than premenopausal women of the same age. Because the incidence of cardiovascular disease in postmenopausal women gradually approaches that in age-matched men, estrogens or progestins (an inclusive term for the natural hormone progesterone and its physiologically active chemical congeners) appear to have a protective effect in premenopausal women. A large, 10-year prospective study supports a cardioprotective effect for estrogens by showing that postmenopausal estrogen replacement therapy reduces both the incidence of coronary heart disease and mortality from cardiovascular disease. **As for progestins, however, there has been little information about a cardioprotective effect until the recent report by Grodstein et al. showing that the risk of coronary heart disease is significantly lower in women who take estrogens and progestins together rather than estrogens alone.**

In small animal models, estrogen administration inhibits the development of experimentally induced atherosclerosis, and in castrated baboons receiving estradiol and progesterone together, there are fewer vascular lesions than in those receiving estradiol alone. Again, however, there has been little evidence of an independent effect of progestins in animal studies, other than an acute effect on vascular tone.

Progesterone inhibits human endothelial cell proliferation through a p53-dependent pathway

The effect of progesterone on proliferation of vascular endothelial cells has been addressed by Vázquez et. al., who showed that progesterone could inhibit the proliferation of vascular endothelial cells and the rate of re-endothelialization, and thus impair vascular repair processes through progesterone receptor dependent pathway [7]. However, the underlying molecular mechanisms are still not clear, and the effect of progesterone on angiogenesis was not addressed in their study. Since endothelial cell proliferation is one of the major events essential for angiogenesis, the finding of the anti-proliferation effect of progesterone on endothelial cells led us to hypothesize that progesterone might also exert an anti-angiogenic activity.

Angiogenesis, the formation of new blood vessels from pre-existing vessels, is required in many physiological and pathological conditions [8, 9]. Normally, vascular proliferation occurs only during embryonic development, and is a very slow process in the adult with a few specific exceptions. The ovary and endometrium are two of the few tissues in the adult organism in which angiogenesis is a prominent feature in normal conditions. **Studies of the regulation of angiogenesis in the primate endometrium suggest that physiological angiogenesis is under the control of sex steroids.** It has been demonstrated that physiological concentrations of estradiol increase VEGF expression in endometrial epithelial and stromal cells [10–12]. **There is a large body of literatures that describes the important role of estradiol in endometrial angiogenesis, but far less is known about the progesterone effect in this aspect.**

Thy-1, a Novel Marker for Angiogenesis Upregulated by Inflammatory Cytokines

Angiogenesis is fundamental to reproduction, fetal development, and tissue repair. However, angiogenesis also plays an important role in the pathogenesis of tumor growth and ophthalmic and rheumatic diseases.¹ Although the sequence of events governing angiogenesis associated with pathological or reparative processes in adults no doubt resembles that associated with developmental processes in embryos, it probably involves additional mechanisms more distinct to adults. In pathological conditions, for example, angiogenesis is thought to be accompanied by, and may possibly require, **inflammation**.² Indeed, **the elaboration of inflammatory cytokines has been shown to induce angiogenesis**, even though the mechanisms regulating this elaboration remain poorly understood.^{3,4}

Thy-1 is a cell-surface glycoprotein that belongs to the **immunoglobulin-like supergene family**.⁵ Originally described as a marker for thymocyte differentiation in mice,⁶ Thy-1 was subsequently found to be expressed highly in neuronal cells.^{7,8} **Variable Thy-1 expression has been observed in other cell types, including vascular endothelial cells.**⁹

有的會在緒論的結尾寫
出本研究的發現

We show in this study that progesterone, the nature hormone, has a direct and specific inhibitory effect on the proliferation of subcultured arterial smooth muscle cells. Under appropriate conditions, subcultured smooth muscle cells are capable of contraction in response to physiologic stimuli and growth factors, although we did not test contractility in the specific subculture studied here. Arterial smooth muscle cells contain abundant progesterone receptors that may mediate this inhibitory effect, and inhibition occurs at a range of progesterone concentrations (5-500 nM) that overlaps the physiologic range of plasma progesterone concentrations in premenopausal women (at day 9 of menstrual cycle, the plasma concentration ranges between 22 and 73 nM; at 34-35 weeks gestation, the evening plasma progesterone value is 507.5 ± 47.7 nM). We also show that levels of cyclin A and E mRNA decline in the progesterone in rat aortic smooth muscle cells, which suggests that progesterone interrupts the cell cycle at the G1/S transition.

Using antibodies specific to Thy-1, we identified it as a cell-surface marker expressed on microvascular endothelial cells during new blood vessel formation. Thy-1 was expressed during pathological and physiological angiogenesis in adult rats but not during embryonic angiogenesis. In cultured microvascular endothelial cells, the inflammatory cytokines interleukin-1 β and tumor necrosis factor- α selectively upregulated Thy-1 expression. Vascular endothelial growth factor, basic fibroblast growth factor, transforming growth factor- β , and platelet-derived growth factor-BB had no effect on Thy-1 expression.

或是在緒論的結尾寫出
本研究的重點與意義

In the present investigation, we studied some antiangiogenic actions of progesterone and examined the underlying cellular and molecular mechanisms in both in vitro and in vivo experiments. These experimental findings reported below highlight certain molecular mechanisms of progesterone-induced inhibition of angiogenesis.

緒論中最好能描述此
研究的緣由

Anti-proliferation effect of 3-amino-2-imino-3,4-dihydro-2H-1,3-benzothiazin-4-one (BJ-601) on human vascular endothelial cells

Structurally, 3-amino-2-imino-3,4-dihydro-2H-1,3-benzothiazin-4-one (BJ-601) is a benzothiazinone derivative (Fig. 1). Previous studies have shown that benzothiazinone can block the voltage-dependent L-type calcium channels [3,4], and inhibit the activity of angiotensin converting enzyme [5]. It has been suggested that such benzothiazinone derivatives may offer some useful medicinal actions including: analgesic, anti-inflammatory, antimicrobial, etc. [6]. Moreover, the benzothiazinone analogues have been shown to inhibit xanthine oxidase activity [7]. However, the anti-angiogenic activity of benzothiazinone and derivatives has not been addressed. **While studying the cytotoxicity of benzothiazinone derivatives, we found that BJ-601 exerted significant inhibition on the growth of human vascular endothelial cells. These findings prompted us to study the anti-angiogenic effect of BJ-601 and its underlying molecular mechanisms.**

Folic acid inhibits endothelial cell proliferation through activating the cSrc/ERK 2/NF- κ B/p53 pathway mediated by folic acid receptor

While investigating medicinal agents capable of restraining the cell cycle and inhibiting the migration in the vascular endothelial cells, we previously identified that BJ-601 (3-amino-2-imino-3,4-dihydro-2H-1,3-benzothiazin-4-one), a benzothiazinone derivate, exerts an anti-proliferation action on cultured human vascular endothelial cells [6], suggesting the potential of BJ-601 as an anti angiogenic agent. In a continuous effort in searching for more powerful anti-angiogenic agents, we found that folic acid exerted the strongest inhibition activity on the growth of HUVEC among a series of BJ-601 derivates. These findings prompted us to study the anti-angiogenic effect of folic acid.

Effects of female sex hormones on folic acid–induced anti angiogenesis

It has been well recognized that folic acid (FA) can help prevent birth defects in the brain and spinal cord. Thus, pregnant women have been recommended to take FA daily. As the side effects caused by FA intake during pregnancy have not been reported, there should be some mechanisms to allow the pregnant mother and the fetus to escape from the FA-induced anti-angiogenic action. Based on the results from our previous studies, we found that FA and progesterone **shared a similar signaling cascade** involved in the upregulation of p53 and inhibition of endothelial cell proliferation. We also observed that **FR could form a complex with female sex hormone receptors. Accordingly, we hypothesize that high concentrations of female sex hormones in the maternal blood might be able to prevent the FA-induced anti-angiogenic activity.** In this study, the molecular mechanism underlying female sex hormones that evoked a prevention effect against the FA-induced anti-angiogenic action was investigated.

**有些重要的 knowledge
background 可放在
Introduction section而不
要放在 Discussion section**

Traditionally, progesterone has been thought to regulate biological effects through binding to its nuclear receptors, progesterone receptor-A or progesterone receptor-B, to alter gene transcription. Lately, a growing body of evidence suggests that progesterone could bind to the progesterone receptor located in the cytoplasm or membrane to initiate a quick acting non-genomic signaling cascade.

緒論中必須提供與本研
究背景直接相關資料

沒有必要在緒論章節列
出所有相關文獻

論文與文章的Introduction不同之處

學位論文沒有篇幅的限制，因此在過去研究的背景介紹可更詳細些