

# CHAPTER I

## INTRODUCTION

*Mucuna collettii* is a Thai traditional plant that widely used as a rejuvenile drug for the native people. It is beleived that *M. collettii* can improve the human physical appearances such as re-growing and promoting black hair, improving flexibility of the body and prolonging life after orally taking the mixture of *M. collettii* powder and honey (Suntara, 1931).

Up to now, numbers of people who concerned themselves about health care increased. Usage of natural products is one of the ways that people used to promote the health care (Sabcharoen, 1998). *M. collettii* is one of the popular herbs that Thai people used for improve their sexual functions, especially, in males (Roengsamran *et al.*, 2001). It is therefore become a subject for research of its effects on reproductive functions in the future these few years.

In 2001, Wuteeraphon *et al.* investigated the effects of *M. collettii* powder suspension at the dosages of 200, 300 and 400 mg/kg/day on sex organs of adult normal male rats for a period of 30 days. The results showed that the oral administration of suspension of *M. collettii* at the dosage of 400 mg/kg/day significantly increased testicular weight ( $p < 0.05$ ) and tended to increased sperm numbers in cauda epididymis and testes. In the same year, Roengsamran and his colleagues (2001) analyzed and found three isolated active compounds from the hole stem of *M. collettii*; kaempferol, quercetin and hopeaphenol. These chemical constituents could highly inhibit cyclic AMP phosphodiesterase enzyme and result in

prolonged penile erection. Kellis and Vickery (1984) reported that quercetin showed a little inhibition of aromatization of androstenedione to estradiol in human placenta. Whitehead and Lacey (2003) reported that quercetin could inhibit progesterone synthesis in human granulosa-luteal cells. However, there are no scientific reports on the effects of kaempferol and hopeaphenol in reproductive system.

The introduction of *M. collettii* into food supplements for both domestic consumption and exportation has been increased rapidly in Thailand. Uncontrolled consumption of *M. collettii* could lead to death which was speculated in a few incidents of heart attack in the past few years (Roengsamran *et al.*, 2001). Although, there are some scientific data that supported the aphrodisiac effects of *M. Collettii*, the information on the toxicity, side-effects and reproductive functions are still not enough. Thus, the basic scientific investigations on this medicinal plants are important and urgently need.

According to the above mentions, there are some published data of *M. collettii* on reproductive organs in male rats and the chemical constituents of *M. collettii* from its stem, but there is no data of *M. collettii* on hormone that it plays the important roles in the regulations of reproductive organs. Thus, our study aims to investigate the effects of *M. collettii* on hormone levels and reproductive organs in rats.

In Thai folklore story, both females and males used this herb to promote their aphrodisiac appearances (Suntara, 1931). Therefore, the animal model used in this study is both sexes of rats. Rats were chosen to be a model in this study because of their small size, easily to control and a short period of reproductive cycle

(Rattanakorn, 2001; Semler, 1992). To clarify whether *M. collettii* has an effects similar to androgenic hormones, the rats were gonadectomized to prevent the confounding effect of the endogenous sex steroid hormones. After gonadectomy for 14 days, the levels of gonadotropins (Gn); follicle stimulating hormone (FSH) and luteinizing hormone (LH) are elevated, and the levels of estradiol (E<sub>2</sub>) and testosterone (T) are decreased (Dalkin *et al.*, 1990; Gay and Bogdanove, 1969; Moulton and Leonard, 1969; Ramirez and McCann, 1965; Swerdloff and Walsh, 1973; Wierman *et al.*, 1990).

The dosages of *M. collettii* used in this study are calculated based on Thai folklore remedy and the pharmacokinetic of drug in rat. As regards to Thai folklore remedy, the ordinary dosage of *M. collettii* for man and woman is one-third of a pepper seed or 60 mg/50kgBW/day or 1.2 mg/kgBW/day. In drug development, the dosage of any substances that treated to experimental animals should be higher than that of human (Berkowitz and Katzung, 2001). The process of metabolism in rats is similar to human, but the metabolic rate is higher and the phenomenon of microsomal enzyme induction is highly induced in liver of rats. In addition, microflora, which can metabolize an orally administered compound, highly distributes in the intestine of rats when compare to human (Berkowitz and Katzung, 2001; Chenglis, 1992). The usage dosage of drug treated to rats is therefore 5-10 times higher than that of human use. From these reasons, the suitable dosage of *M. collettii* in this experiment is 10 mg/kg/day. However, to know whether the effect of *M. collettii* is depended on doses, the concentrations of *M. collettii* at 10-time lower and higher than 10 mg/kg/day, that is 1 and 100 mg/kg/day, were also used in this study.

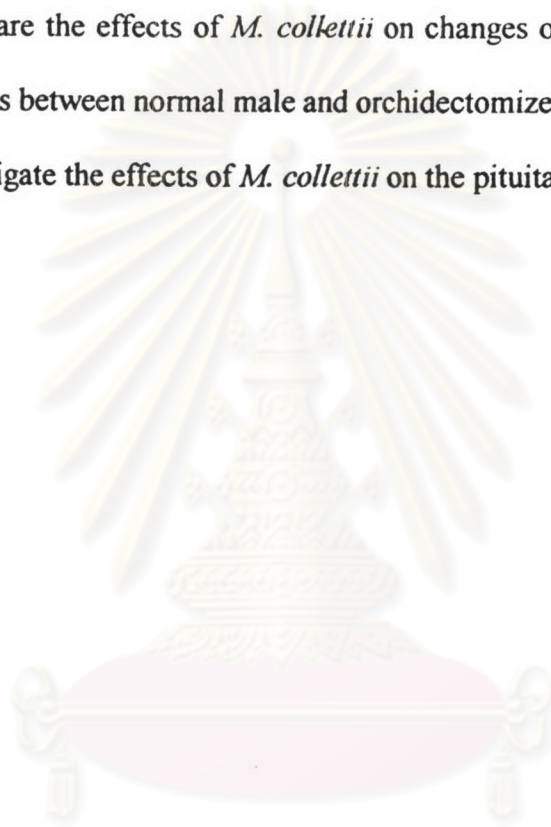


Moreover, to identify exactly this herb has the effects similar to the androgenic hormones, testosterone propionate was used as a positive control for this study. There are reports that testosterone propionate approximately 300  $\mu\text{g}/100\text{gBW}/\text{day}$  in 0.2 ml of sesame oil or more can suppress serum LH levels (Ramirez and McCann, 1965; Swerdloff and Walsh, 1973; Wierman *et al.*, 1990) and FSH levels (Beyer *et al.*, 1974; Gay and Bogdanove, 1969; Swerdloff and Walsh, 1973; Wierman *et al.*, 1990) in male and female rats. In addition, testosterone propionate administration at least 50  $\mu\text{g}/300\text{gBW}/\text{day}$  can decrease the testicular weight (van Roijen *et al.*, 1997), increase the weights of epididymis and seminal vesicle, increase serum T levels and decrease testicular T levels by dose-dependent in male rats (Gay and Bogdanove, 1969; Ramirez and McCann, 1965; Swerdloff and Walsh, 1973; van Roijen *et al.*, 1997). Moreover, testosterone propionate at least 500  $\mu\text{g}/200\text{gBW}/\text{day}$  can decrease ovarian weight (Beyer *et al.*, 1974), increase uterine weight (Garcia and Rochefort, 1977; Ruth and Ruth, 1975; Schmidt *et al.*, 1976) and produce unestrus cycles in normal female rats (Beyer *et al.*, 1974). Therefore, testosterone propionate at the dosage of 600  $\mu\text{g}/100\text{gBW}/\text{day}$  in 0.2 ml of sesame oil was chosen to ensure the suppressive effects on pituitary-gonadal axis in this study.

On principle of physiology, homeostasis is interfered when the body receives any substances. Therefore, orally treated rats with the various dosages of the powder suspension of *M. collettii* may disturb the homeostasis of hypothalamic-pituitary-gonadal axis. The serum FSH, LH,  $\text{E}_2$  (in females) and T (in males) levels were analyzed in this study.

The aims of this study are as follows;

1. To study the effects of various dosages of *M. collettii* on serum hormone levels and reproductive organs in both sexes of rats.
2. To compare the effects of *M. collettii* on changes of Gn levels and accessory sex organs between normal female and ovariectomized female rats.
3. To compare the effects of *M. collettii* on changes of Gn levels and accessory sex organs between normal male and orchidectomized male rats.
4. To investigate the effects of *M. collettii* on the pituitary-gonadal axis.



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