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Some Physiological and Behavioral Effects of Ghrelin Hormone in White Rats

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Abstract

This study was carried out to estimate the ghrelin-like effects induced by feed restriction and *Syzygium aromaticum* (clove) supplementation on reproductive system of female *Sprague dawley* rats during estrous cycle and pregnancy. In the 1st experiment (estrous experiment): seventy-two adult female *Sprague dawley* rats were equally divided into 4 groups: control group was fed on a standard ration (15g/animal/day), feed restricted group fed on (7.5g/animal/day) and two clove-supplemented groups were fed on a standard ration to which clove powder was added at a rate (15 and 30 mg/kg animal/day), respectively. In the 2nd experiment (pregnancy experiment): one-hundred adult female pregnant *Sprague dawley* rats equally divided into 5 groups: control group fed on a standard ration (15g/animal/day) then increased to (20g/animal/day) from the 14th day of gestation, feed restricted group received 50% of the daily standard ration, two clove-supplemented groups were fed on standard ration to which clove powder was added at a rate (15 and 30 mg/kg animal/day), respectively and the last 5th control feed restricted group received standard ration before the pregnancy and 50% of the daily standard ration after induction of pregnancy. The results revealed that feed restriction decreased body weight while dietary clove increased body weight. Both feed restriction and clove supplementation stimulated the secretion of endogenous ghrelin which was negatively reflected on reproductive hormones (estradiol, progesterone, follicle-stimulating hormone (FSH), luteinizing hormone (LH) and thyroid stimulating hormone (TSH) levels and consequently resulted in irregularity of estrous cycle of feed restricted animals and ended by a persistent diestrus in the 1st experiment, decrease in pregnancy percentage, increase in resorbed sites and pre-implantation sites as well as decrease in fetal weights and lengths in the 2nd experiment. In addition, q-RT PCR showed a significant increase in the gastric ghrelin expression of feed restricted and clove supplemented rats and a significant decrease in the ovarian ghrelin expression during estrus cycle and pregnancy.

Key words: Ghrelin, feed restriction, *Syzygium aromaticum* (clove), estradiol, progesterone, FSH, LH, TSH, gene expression, stomach, ovary, estrous cycle, pregnancy rats.

Dedication

This thesis work is dedicated to the soul of my mother, who has always loved me unconditionally and whose good example has taught me to work hard for the things that I aspire to achieve.

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LIST OF ABBREVIATION

Abb.	Title
AMPK	Adenosine Monophosphate-Activated Kinase
ACTH	Adrenocorticotropic Hormone
AgRP	Agouti-Related Peptide
Akt	Protein Kinase-B
BMI	Body Mass Index
cDNA	Complementary DNA
CL	Corpora Lutea
CU-IACUC	Ethics Committee of Cairo University-Institutional Animal Care & Use Committee
DI	Liver deiodinase type-I
ERF	Eugenol-Rich Fraction
E ₂	Estradiol Hormone
FSH	Follicle Stimulating Hormone
GnRH	Gonadotropin Releasing Hormone
GPC-R	G-Protein Coupled Receptor
GPC-R39	G-Protein Coupled-Receptor 39
GH	Growth Hormone
GHS-R	Growth Hormone Secretagogue Receptor
GHRH	Growth Hormone-Releasing Hormone.
Ghrl	Ghrelin Hormone
PYY	Gut Hormone Peptide
hCG	human Chorionic Gonadotropin
HE	Hyperghrelinaemia condition

HPG-axis	hypothalamic-pituitary gonadal axis
HPT-axis	Hypothalamus-Pituitary-Thyroid axis
IGF-1	Insulin like growth factor-1
IGFBP-1	Insulin-like growth factor-binding protein-1
ICV	Intra-cerebroventricular
Kiss1	Hypothalamic Kiss-peptin1
KLF-4	Krüppel-Like Factor 4
LH	Luteinizing Hormone
mRNA	messenger RNA
MAPK	Mitogen-Activated Protein Kinase
MPO	Myeloperoxidase
NPY	Neuropeptide Y
GDF9	oocyte-specific growth factor
PGF2 α	Prostaglandin F2alpha
POMC	Pro-opiomelanocortin
PVN	Para-Ventricular Nucleus
PRL	Prolactin Hormone
P ₄	Progesterone Hormone
PKA	Protein Kinase-A
7TM	seven Transmembrane Domain
STAT3	Steroidogenic Acute Regulatory Protein Expression
StAR	Signal Transducer and Activator of Transcription 3
TRH	Thyrotropin-releasing hormone
TSH	Thyroid Stimulating hormone
α -MSH	α -Melanocyte-Stimulating Hormone.

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Chapter (1)

1.INTRODUCTION

1. INTRODUCTION

Recently, attention has been paid to the energy balance and factors involved in its regulation specially hormones. These factors are classified into three main groups: homeostatic, environmental and behavioural processes. One of the most important elements which plays a critical role in the regulation of appetite and energy balance is ghrelin hormone which was firstly discovered by **Kojima** and his **colleagues** in rat stomach. This hormone was identified as the endogenous ligand, a peptide hormone containing 28 amino acids with C-terminal Arg. It is secreted mainly by the stomach, although its expression has been detected in many other organs such as kidneys, adrenal glands, thyroid gland, breast, ovary, placenta, testis, prostate, liver, gall bladder, lung, skeletal muscles, myocardium, skin, and bone (**Barreiro and Tena-Sempere, 2004**). Ghrelin exerts wide physiological actions throughout the body, including regulation of sleep (**Seoane et al., 2004**), regulation of cardiovascular functions (**Iglesias et al., 2004**), regulation of gastrointestinal motility (**Peeters, 2006**), production of proinflammatory cytokines (**Taub, 2007**), initiation of cell proliferation (**Granata et al., 2007**), stimulation of feed intake and regulation of blood glucose level (**De Vriese and Delporte, 2008**) and increase body weight gain (**Castañeda et al., 2010**). It also controls several aspects of female reproductive physiology and behavioral functions through endocrine and autocrine/paracrine pathways. In this sense, normal timing of puberty can be delayed if ghrelin levels are persistently elevated as putative signal for energy insufficiency (**Tena-Sempere, 2007a**). Ghrelin shows