



***EFFECTS OF DIETARY SUPPLEMENTATION WITH LOVASTATIN ON  
FEED DIGESTIBILITY, METHANE EMISSION, CARCASS  
CHARACTERISTICS AND MEAT QUALITY OF GOAT***

**SANI GARBA**

**IPTSM 2019 1**



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By

**SANI GARBA**

**Thesis Submitted to the School of Graduate Studies, Universiti Putra Malaysia,  
in Fulfillment of the Requirements for the Degree of Doctor of Philosophy**

**October 2018**

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## **DEDICATION**

This PhD work is dedicated to my dear wife, Hajara who remains willing to engage with the struggle and ensuing discomfort during my absence throughout the period of this study. A very special thank you for your practical and emotional support for being not only dedicated but also a loyal partner.

Thanks to dear Shu'aibu, Sabir, Fadila and Fatima, for being so tolerant - even when being 'without Dad' was tough. This work is for, and because of your future development. It is dedicated to all our journeys in learning to thrive.



Abstract of thesis presented to the Senate of Universiti Putra Malaysia in fulfilment of the requirement for the degree of Doctor of Philosophy

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**October 2018**

**Chairman : Associate Professor Awis Qurni Sazili, PhD**  
**Institute : Tropical Agriculture and Food Security**

Efforts including the use of feed additives and supplements to mitigate rumen methanogenesis were intensively researched but their low efficacy and sustainability have resulted in limited acceptance at farm level. Therefore, there is a need for the development of an effective CH<sub>4</sub> mitigating agent which is not only cost effective but safer to both animals and consumers as well. Statin reduces the level of low-density lipoprotein cholesterol by effectively inhibiting 3-hydroxy-3-methylglutaryl coenzyme A (HMG-CoA) reductase and has also been reported to reduce methanogenesis and thus enteric CH<sub>4</sub> production. However, it has been reported that administration of statin can cause side-effects such as myopathy. This research/thesis evaluated the effect of feeding naturally-produced lovastatin on feed digestibility, CH<sub>4</sub> emission, carcass characteristics, meat quality, accumulation of lovastatin residues and possible skeletal muscle myopathy in goats fed with different dosages of naturally-produced lovastatin over three measuring periods (4-, 8- and 12-weeks). Therefore, experiments were conducted using four dietary treatments containing 0 (Control), 2 mg (Low), 4 mg (Medium) and 6 mg (High) per kg BW of naturally-produced lovastatin fed to the experimental goats for 12 consecutive weeks under the same management conditions. In the first experiment, effective dosage of naturally-produced lovastatin to reduce CH<sub>4</sub> emission in long-term mitigation of emission of greenhouse gasses into the atmosphere using palm kernel cake (PKC) as a substrate incubated with *Aspergillus terreus* was determined. The results showed that lovastatin had no effect on feed digestibility. Enteric CH<sub>4</sub> emissions per unit dry matter intake (DMI) decreased by 11% and 20.4%, respectively, for the 2 and 4 mg/kg BW groups and no further decrease in CH<sub>4</sub> emission thereafter with higher lovastatin supplementation and minor effect on rumen microbiota. The goats were slaughtered after 12 weeks of the feeding trial according to the halal procedure. Experiment two investigated the blood and histological parameters of the goats fed different dosages

of naturally-produced lovastatin for any effect on animals' physiology or health. No significant difference ( $p < 0.05$ ) in all the blood parameters tested except triglycerides (cholesterol, LDL, HDL) and granulocytes (basophil and eosinophil). However, histological study showed supplementation of naturally-produced lovastatin at 4 mg/kg BW and 6 mg/kg BW causes changes in histologic features. Thus, indicating the possibility of muscle myopathy. In order to safeguard public health, meat products must not contain residues associated with feed and drug residues that might constitute a health hazard. Thus, third experiment was conducted using HPLC and LCMS/MS methods to detect lovastatin residues. Lovastatin residues were detected in Longissimus thoracis et lumborum (LTL) muscle; liver and kidney samples from goats fed 6 mg lovastatin/kg BW and the residues were range between 0.01-0.03  $\mu\text{g/g}$  which is far below the level recommended for hyper-cholesterol treatment in humans. The fourth experiment aimed at investigating the carcass characteristics, physico-chemical properties, storage stability and cholesterol content of meat from goats fed with different dosages of naturally-produced lovastatin. No differences were found in all the parameters measured except for full LW, hot and cold carcass weight, color, shear force and cholesterol content among the treatment groups. Meats in the medium and high treatments were more tender and had lower cholesterol levels. Supplementation of naturally-produced lovastatin at 4 mg/kg BW dose can effectively mitigate methane production and reduce cholesterol level at what can be regarded as safe for consumers.

Abstrak tesis yang dikemukakan kepada Senat Universiti Putra Malaysia sebagai memenuhi keperluan untuk ijazah Doktor Falsafah

**KESAN- KESAN SUPLEMEN MAKANAN DENGAN LOVASTATIN  
TERHADAP KEBOLEHCERNAAN MAKANAN, PELEPASAN METANA,  
CIRI-CIRI KARKAS DAN KUALITI DAGING KAMBING**

Oleh

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**Oktober 2018**

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Usaha seperti penggunaan aditif dan suplemen makanan untuk mengurangkan metanogenesis rumen telah dikaji secara intensif tetapi keberkesanan dan kesinambungan yang rendah telah mengakibatkan penerimaan yang terhad di peringkat ladang. Oleh itu, agen pengurangan CH<sub>4</sub> yang berkesan perlu dibangunkan di mana ia bukan sahaja mempunyai penggunaan kos yang efektif tetapi juga selamat untuk haiwan dan pengguna. Statin mengurangkan tahap kolesterol lipoprotein berketumpatan rendah dengan cara menghalang reduktase 3-hydroxy-3-methylglutaryl coenzyme A (HMG-CoA) dan juga telah dilaporkan dapat mengurangkan metanogenesis dan seterusnya pengeluaran CH<sub>4</sub>. Walau bagaimanapun, terdapat laporan di mana penggunaan statin boleh menyebabkan kesan sampingan seperti myopathy. Tesis ini menilai kesan pemberian lovastatin yang dihasilkan secara semulajadi terhadap pembebasan CH<sub>4</sub>, ciri-ciri karkas, kualiti daging, pengumpulan sisa lovastatin dan kemungkinan terjadinya myopathy otot rangka pada kambing yang diberi makan lovastatin yang dihasilkan secara alami pada paras yang meningkat dalam tiga tempoh pengukuran (4-, 8- dan 12-minggu). Untuk mencapai ini, eksperimen dijalankan dengan menggunakan empat rawatan diet yang mengandungi 0 mg (Kawalan), 2 mg (Rendah), 4 mg (Sederhana) dan 6 mg (Tinggi) per kg BW lovastatin yang dihasilkan secara alami dimana keempat-empat rawatan diet ini diberi makan kepada kambing-kambing eksperimentasi selama 12 minggu berturut-turut di bawah kawalan pengurusan yang sama. Dalam eksperimen pertama, dos efektif lovastatin dihasilkan secara semulajadi untuk mengurangkan pelepasan CH<sub>4</sub> dalam mitigasi jangka panjang pelepasan gas rumah hijau ke atmosfera menggunakan kek empan sawit (PKC) sebagai substrat yang diinkubasi dengan *Aspergillus terreus* ditentukan. Keputusan eksperimen menunjukkan bahawa lovastatin tidak mempunyai kesan terhadap pencernaan makanan. Pelepasan enterik CH<sub>4</sub> bagi setiap pengambilan bahan kering (DMI) telah menurun sebanyak 11% dan 20.4%, masing-masing untuk

kumpulan 2 dan 4 mg/kg manakala suplementasi lovastatin pada kadar yang lebih tinggi menunjukkan tiada pengurangan dalam pelepasan CH<sub>4</sub>, dan juga memberi kesan yang sedikit terhadap microbiota rumen. Kambing-kambing tersebut disembelih secara halal setelah 12 minggu pemberian makanan percubaan. Eksperimen kedua dijalankan bagi menyiasat parameter darah dan histologi kambing yang diberi makan lovastatin yang dihasilkan secara semulajadi dengan kadar meningkat untuk mencari sebarang kesan pada fisiologi atau kesihatan haiwan. Tiada perbezaan yang ketara ( $p < 0.05$ ) dalam semua parameter darah yang diuji kecuali trigliserida (kolesterol, LDL, HDL) dan granulosit (basophil dan eosinophil). Walau bagaimanapun, kajian histologi menunjukkan suplementasi lovastatin yang dihasilkan secara semulajadi pada 4 mg/kg BW dan 6 mg/kg BW menyebabkan perubahan dalam ciri-ciri histologi. Seterusnya menunjukkan tanda-tanda kemungkinan terjadinya myopathy otot. Untuk melindungi kesihatan awam, produk daging tidak boleh mengandungi residu yang berkaitan dengan sisa makanan dan dadah yang boleh membawa kepada kemudaratan kesihatan. Oleh itu, eksperimen yang ketiga telah dijalankan dengan menggunakan kaedah HPLC dan LCMS/MS. Sisa-sisa lovastatin dikesan di otot *Longissimus thoracis et lumborum* (LTL); sampel hati dan buah pinggang dari kambing yang diberi makan 6 mg lovastatin/kg BW dan bacaan antara 0.01-0.03 µg/g didapati mana paras ini berada pada tahap yang rendah bagi disyorkan untuk rawatan hiper-kolesterol pada manusia. Eksperimen yang keempat bertujuan untuk menyiasat ciri-ciri karkas, sifat fiziko-kimia, kestabilan penyimpanan dan kandungan kolesterol daging dari kambing yang diberi makan dengan pelbagai tahap lovastatin yang dihasilkan secara semulajadi. Tiada perbezaan yang ditemui dalam semua parameter yang diukur kecuali untuk LW penuh, berat badan hangat dan dingin, daya potong dan kandungan kolesterol di kalangan kumpulan rawatan. Daging daripada rawatan sederhana dan tinggi didapati lebih lembut dan mempunyai tahap kolesterol yang lebih rendah. Suplementasi lovastatin yang dihasilkan secara alami pada dos 4 mg/kg BW berkesan dalam mengurangkan pengeluaran metana dan mengurangkan tahap kolesterol di mana hal ini dianggap sebagai selamat bagi pengguna.



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This thesis was submitted to the Senate of the Universiti Putra Malaysia and has been accepted as fulfilment of the requirement for the degree of Doctor of Philosophy. The members of the Supervisory Committee were as follows:

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## CHAPTER 1

### GENERAL INTRODUCTION

Demand for livestock products is forecast to increase due to the growing demands for meat and milk as a result of human population growth and an improved standard of living globally (Bodirsky *et al.*, 2015). Meeting this demand for food, whilst reducing the environmental impact of livestock, is a great challenge globally. A substantial rise in agricultural greenhouse gases (GHG) emissions is anticipated if livestock production continues in the current trend, so there is need for new strategies to both mitigate GHG emissions and increase productivity from livestock (Eckard *et al.*, 2010; Bennetzen *et al.*, 2016). Efforts are being made by governments around the world to develop mitigations to reduce methane (CH<sub>4</sub>) emissions from ruminant livestock. However, livestock producers are unlikely to adopt these strategies if the CH<sub>4</sub> mitigating strategies reduce animal production and, hence, profitability (Grainger and Beauchemin, 2011). One promising approach is the use of feed additives and supplements as modulators of rumen methanogenesis. Through the interference with membrane synthesis, lovastatin can inhibit the growth of methanogenic Archaea in the rumen without adverse effects on other cellulolytic bacteria (Miller and Wolin, 2001) and, in this way, mediates the reduction in CH<sub>4</sub> release into the environment. Using crop residue (such as rice straw) to produce lovastatin besides mitigating enteric methane emission also enhanced nutrients digestibility and thus overall animal productivity (Goldstein and Brown, 1990; Jahromi *et al.*, 2013b, Azlan *et al.*, 2017). In addition, statins reduce the level of low-density lipoprotein cholesterol by effectively inhibiting 3-hydroxy-3-methylglutaryl coenzyme A (HMG-CoA) reductase, an enzyme that catalyzes both enteric CH<sub>4</sub> production and cholesterol production (Jahromi *et al.*, 2013b). Despite the positive effect of statin to reduce enteric CH<sub>4</sub> production, it was reported (Evans and Rees, 2002; Staffa *et al.*, 2002; Thompson *et al.*, 2003; Rosenson, 2004) that administration of statin may cause side-effects such as myopathy with varied clinical symptoms ranging from mild myalgia to myositis and fatal rhabdomyolysis. Diet (Casey and Webb, 2010) including dietary supplementation (Oliveira *et al.*, 2015) are pre-slaughter interventions for the manipulation of both carcass and meat quality traits in ruminants. This thesis assessed the effects of supplementing naturally-produced lovastatin on methane emission, carcass and physico-chemical characteristics and lovastatin residue in meat, and possible myotoxicity using goats as the animal model.

The objectives of this study are:

- I. To determine the effective dosage of naturally produced lovastatin to minimize CH<sub>4</sub> emission in long-term mitigation of emission of greenhouse gasses into the atmosphere using palm kernel cake (PKC) as a substrate incubated with *Aspergillus terreus*.
- II. To evaluate blood parameters, histological structure of goats *Longissimus thoracis et lumborum* (LTL) muscle, animal welfare and health status of goats fed different dosages of naturally-produced lovastatin.
- III. To detect and quantify residues of lovastatin in the *Longissimus thoracis et lumborum* (LTL) muscle and edible organs.
- IV. To determine the influence of different dosages of dietary supplementation of naturally- produced lovastatin on carcass characteristics, meat quality traits, lipid oxidation and cholesterol level in goats.

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