UNIVERSITI PUTRA MALAYSIA

EFFICACY OF VITAMIN E AND SELENIUM SUPPLEMENTATION IN THE PREVENTION AND TREATMENT OF SIGNAL GRASS (BRACHIARIA DECUMBENS STAPF.) TOXICITY IN SHEEP

AJWAD AWAD MUHAMMAD

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By

AJWAD AWAD MUHAMMAD

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

December 2011

In the name of ALLAH the Most Gracious and Merciful

With appreciation and respect,
This thesis is dedicated

To the spirit of my father,
who inspired me with confidence and ambitions.

To my lovely mother, brothers and sisters,
who made this work endurable.

To my wife, sons and daughter,
for their peerless support and understanding.

To my supervisor,
who ensured it all worthwhile.

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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Chairman: Noordin Mohamed Mustapha, PhD

Faculty: Veterinary Medicine

Continuous incidence of *Brachiaria decumbens* intoxication outbreaks arises due to ineffective strategies in treating and preventing its aftermath in the global small ruminant industry. Previous conducted studies focusing on the prevention yielded with limited success. Improved usage of *B. decumbens* for livestock production requires better approach to reduce losses caused by its toxic effects. In this thesis, studies conducted were based on the principle dogma of using certain antioxidants both in prevention and treatment of *B. decumbens* intoxication in sheep.

Following confirmation of oxidative stress (feeding of *B. decumbens* alone) in the pathogenesis of this toxicity, the role of vitamin E and selenium combination in preventing and treating toxicity was mounted.

A total of 36 local indigenous sheep were used in two sets of experiments. In all experiments, sheep receiving *B. decumbens* were fed the grass obtained via cut and

carry either alone or with vitamin E+selenium 14 days before and in the first day of start feeding or injected subcutaneously with combination of vitamin E+selenium on the 1st and 3rd day of the first clinical sign appearance of *B. decumbens* intoxication.

Classical clinical signs of *B. decumbens* intoxication were monitored. Blood and pertinent tissues were collected at necropsy. The liver and kidney function tests, pertinent indicators reflecting lipid peroxidation status and antioxidant defenses were assayed. Furthermore, some liver metabolizing enzymes and pathological studies both at cellular and ultrastructural levels were conducted too.

Clinical signs of photosensitisation jaundice and submandibular oedema and lesions of hepatocytic necrosis, renal hydropic degeneration and/or coagulative necrosis and brain vacuolations due to status spongiosus of the white matter (demyelination) were noticed in sheep fed *B. decumbens* alone.

An impairment of the antioxidant defense system and involvement of lipid peroxidation was confirmed in all *B. decumbens* fed sheep except those receiving vitamin E plus selenium either as a prophylaxis or treatment. Obviously, selenium and vitamin E function synergistically to protect against cellular damage by intermediate reactive species. Vitamin E, an integral component of the cell membrane, is in perfect position to disrupt the lipid peroxidation process by quench free radicals capable of initiating and propagating lipid peroxidation such as alkoxy and alkyl peroxy radicals and have been shown to affect the activity and induction of the microsomal P-450. Selenium as an essential constituent of the glutathione peroxidase (Se-GSH-Px) active site reduces hydrogen peroxide, as well as other

hydroperoxides to less reactive water and alcohols, respectively. Therefore, the supplementation of vitamin E as α-tocopherol acetate+sodium selenite is effective in blocking the development of *B. decumbens* intoxication in sheep by potentiating the cells' ability to cope with oxidative stress and thus block membrane lipid peroxidation that can disrupt cell compartmentalization and function during *B. decumbens* ingestion. Therapeutically, the conducted study showed that supplementation with vitamin E and selenium is efficacious in alleviating the toxicity of *B. decumbens* in sheep.

Key words: Sheep, *Brachiaria decumbens*, oxidative stress, hepatotoxicity, vitamin E plus selenium

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

KEBERKESANAN PEMBERIAN VITAMIN E DAN SELENIUM DALAM PENCEGAHAN DAN RAWATAN KETOKSIKAN RUMPUT SIGNAL (*BRACHIARIA DECUMBENS* STAPF.) PADA BIRI-BIRI

Oleh

AJWAD AWAD MUHAMMAD

Disember 2011

Pengerusi: Noordin Mohamed Mustapha, PhD

Fakulti: Perubatan Veterinar

Peletusan insidens ketoksikan *Brachiaria decumbens* masih berterusan akibat dari strategi yang kurang berkesan dalam pencegahan dan rawatan dalam global industri ruminan kecil. Kajian sebelumnya yang tertumpu terhadap pencegahan tidak begitu berjaya. Penggunaan *B. decumbens* yang lebih baik untuk pengeluaran ternakan memerlukan pendekatan yang lebih baik untuk mengurangkan kerugian akibat ketoksikan. Dalam tesis ini, kajian dijalankan berdasarkan dogma menggunakan anti-pengoksida khusus dalam pencegahan dan rawatan ketoksikan pada biri-biri.

Lanjutan dari pengesahan peranan tegasan oksidatif (pemakanan *B. decumbens* sahaja) dalam patogenesis ketoksikan ini, peranan vitamin E dan selenium samada berasingan atau gabungan dalam mencegah dan merawat ketoksikan dijalankan.

Sebanyak 36 ekor biri-biri tempatan digunakan dalam dua set ujikaji. Dalam semua ujikaji, biri-biri yang menerima *B. decumbens* diberi makan secara potong dan

angkut samada berasingan atau bersama dengan vitamin E+selenium 14 sebelum dan pada hari pertama memakan atau disuntik secara subkutis dengan gabungan vitamin E+selenium pada hari pertama dan ketiga penjelmaan petanda klinikal ketoksikan *B. decumbens*.

Petanda utama ketoksikan *B. decumbens* dipantau. Darah dan tisu berkaitan diambil ketika nekropsi. Ujian fungsi hati dan ginjal, penanda berkaitan status pengoksidaan lipid dan pertahanan anti-oksid diasai. Tambahan, beberapa enzim metabolisme hati dan kajian patologi juga dibuat pada peringkat sel dan ultrastruktur.

Petanda klinikal fotopekaan, jaundis, edema submandibel dan lesi nekrosis hepar, degenerasi hidrofik dan/atau nekrosis koagulatif renal dan pemvakoulan pada jisim putih akibat status spongiosus (penyahmielinan) pada otak dikesan pada biri-biri yang hanya diberi makan *B. decumbens* sahaja.

Gangguan sistem pertahanan anti-oksid dan penglibatan pengoksidaan lipid disahkan pada semua biri-biri yang menerima *B.* decumbens kecuali yang dipra-suntik dengan vitamin E+selenium samada sebelum atau selepas ketoksikan. Jelasnya, selenium and vitamin E berfungsi secara sinergi untuk melindungi kerosakan sel oleh spesis perantara. Justeru, pemberian vitamin E dan selenium berupaya melindungi sel dari kerosakan akibat ketoksikan *B. decumbens* samada sebagai pecegah atau dalam rawatan.

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I certify that a Thesis Examination Committee has met on (**23 december 2011**) to conduct the final examination of (Ajwad Awad Mohammed Assumaidaee) on his thesis entitled **"The Efficacy of Vitamin E and Selenium Supplementation in the Prevention and Treatment of Signal Grass (*Brachiaria decumbens*) Toxicity in Sheep"** in accordance with the Universities and University Colleges Act 1971 and the Constitution of the Universiti Putra Malaysia [P.U.(A) 106] 15 March 1998. The Committee recommends that the student be awarded the Degree of (Doctor of Philosophy).

Members of the Thesis Examination Committee were as follows:

Mohamed Ali Rajion, PhD
Professor
Faculty of Veterinary Medicine
Universiti Putra Malaysia
(Chairman)

Dato' Sheikh Omar Abdul Rahman, MRCVS
Professor
Faculty of Veterinary Medicine
Universiti Putra Malaysia
(Internal Examiner)

Md Sabri Mohd Yusoff, PhD
Lecturer
Faculty of Veterinary Medicine
Universiti Putra Malaysia
(Internal Examiner)

Gerald E. Duhamel, PhD
Professor
Department of Biomedical Sciences College of Veterinary Medicine
Cornell University
United States of America
(External Examiner)

SEOW HENG FONG, PhD
Professor and Deputy Dean
School of Graduate Studies
Universiti Putra Malaysia

Date:

This thesis was submitted to the Senate of 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:

Noordin Mohamed Mustapha, PhD
Professor
Faculty of Veterinary Medicine
Universiti Putra Malaysia
(Chairman)

Mohd Zamri Saad, PhD
Professor
Faculty of Veterinary Medicine
Universiti Putra Malaysia
(Member)

Jasni Sabri, PhD
Associate Professor
Faculty of Veterinary Medicine
Universiti Putra Malaysia
(Member)

BUJANG BIN KIM HUAT, PhD
Professor and Dean
School of Graduate Studies
Universiti Putra Malaysia

Date:

DECLARATION

I declare that the thesis is my original work except for quotations and citations which have been duly acknowledged. I also declare that it has not been previously, and is not concurrently, submitted for any other degree at Universiti Putra Malaysia or at any other institution.

AJWAD AWAD MUHAMMAD

Date: 23 December 2011

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Al	aluminum
Alb	albumin
ALT	alanine aminotransferase
AST	aspartate aminotransferase
a-Toc	α-Tocopherol
ATPase	Adenosine triphosphatase
BCA	Bicinchoninic Acid Assay
Bd	group feed with *Brachiaria decumbens*
BHT	butylated hydroxyl toluene
BSA	bovine serum albumin
BSP	bromosulphopthalein
BUN	blood urea nitrogen
C	carbon
CO	carbon monoxide
Ca^{2+}	calcium ion
CB	conjugated (direct) bilirubin
Cd	cadmium
CD36	cluster of Differentiation 36
CIAT	International Center for Tropical Agriculture
CDNB	1-Chloro-2,4-dinitrobenzene
cm	centimeter
Creat.	creatinine
Cu	copper

CYP	cytochrome oxidase
DCT	distal convoluted tubule
DDSA	dodecenyl succinic anhydride
DHP	di-hydroxy-4 (H) pyridone
DM	dry matter
DNA	deoxy ribonucleic acid
DTNB	dithiobis 2-nitrobenzoic acid
DZN	diazinon
EDTA	ethylene diamine tetra acetic acid
ES	group injected with vitamin E+selenium
E-SOD	erythrocyte- superoxide dismutase
FAO	food and agricultural organization
FDA	Food and Drug Administration
Fe	iron
g	gram
g	units of relative centrifugal force (times gravity or × *g*)
	$g = (1.118 \times 10^{-5})\ R\ S^2$ where R is the radius of the rotor in centimeters, and S is the speed of the centrifuge in revolutions per minute
GGT	γ-glutamyl transferase
GLDH	glutamate dehydrogenase
GSH-Px	glutathione peroxidase
GSSG	oxidized glutathione
GST	glutathione S- transferase
ha	hectare

H&E	haematoxylin and eosin staining
H_2O_2	hydrogen peroxide
Hb	haemoglobin
HPS	hepatogenous photosensitisation syndrome
ID	identity document
IgG	immunoglobulin G
IU	international unit
K	potassium
KDa	kilo Dalton
kg	kilogram
kg/ha	kilogram per hectare
L	liter
LSD	Least Significant difference test
M	molar
MARDI	Malaysian Agriculture Research and Development Institute
MDA	malondialdehyde
Me Hg	methyl mercury
MFOs	mixed function oxidases system
M.g	mega gram = 1000 kg = tonne
Mg	magnesium
mg	milligram
mg.Hb	per milligram haemoglobin
ml	millitre
mm	millimeter
mM	millimolar

Mn	manganese
MNA	Methyl Nadic Anhydride
MSc	Master of Science
MWt	molecular weight
N	nitrogen
NADH	nicotinamide adenine dinucleotide
NADPH oxidase	nicotinamide adenine dinucleotide phosphate-oxidase
NADPH	reduced nicotinamide adenine dinucleotide
NaN_3	sodium azide
NaOH	sodium hydroxide
n-BDMA	n-Benzyl Dimethyl Amine
NF-kappa B	nuclear factor kappa B
NH_3	ammonia
nm	nanometer
nmol	nanomolar
No.	number
O.D	optical density
P	phosphorus
p	probability
PA	pyrrolizidine alkaloids
PAS	Periodic Acid-Schiff staining
Pb	lead
PBS	phosphate buffer saline
PCT	proximal convoluted tubule
PCV	packed cell volume

PEG	poly ethylene glycol
PhD	Doctor of Philosophy
PPAR	peroxisome proliferator-activated receptor
PUFA	poly unsaturated fatty acid
PXR	pregnane X receptor
RBC	red blood cell
rER	rough endoplasmic reticulum
rGSH	reduced glutathione
ROS	reactive oxygen species
rpm	revolutions per minute
SQ	subcutaneous injection
SD	standard deviation
SDS	sodium dodecyl sulphate
Se	selenium
sec	second
SeCys	selenocysteine
SeMet	selenomethionine
sER	smooth endoplasmic reticulum
SOD	superoxide dismutase
spp.	species
SPSS	statistical package for the social sciences
SRL	specific root length
TB	total bilirubin
TBA	thiobarbituric acid
TBARS	thiobarbituric acid reactive substance

TEP	tetraethoxypropane
tGSH	total glutathione
TP	total protein
UCB	unconjugated (indirect) bilirubin
UDP-	uridine 5'-diphospho-
UPM	Universiti Putra Malaysia
Ur	urea
USA	United States of America
UV	ultra violet
UVEDCO	United Veterinary Drugs Industrial Company
V	vanadium
WR	working reagent
ww	wet weight
X±SD	mean±standard deviation
Zn	Zinc
α-tocopherol acetate	alpha-tocopherol acetate (vitamin E)
α-TTP	alpha-tocopherol transporting protein
ß	beta
γ	gamma
°C	degree Celsius
%	percentage
$^{\bullet}O_2^-$	superoxide anion
$^{\bullet}OH$	hydroxyl radical
µl	microliter
µmol	micromolar

CHAPTER 1

GENERAL INTRODUCTION

Hepatogenous photosensitisation syndrome (HPS) of livestock is economically important problem in various parts of the world. Many hepatogenous photosensitisation disorders are associated with ingestion of plants containing steroidal saponins (Mathews, 1937; Henrici, 1952; Ender, 1955). Common features of all these diseases are their sporadic occurrence, the difficulty of reproducing signs of the diseases during dosing experiments and the fact that the plants seem to be only occasionally toxic to grazing animals (Flaoyen, 1996). Another pathognomic criterion of HPS is the accumulation of insoluble Ca^{2+} salts of episarsasapogenin or epismilagenin glucuronides in liver cells and bile ducts (Holland *et al*., 1991; Miles *et al*., 1991, 1992a,b ; 1993).

Brachiaria decumbens (signal grass) intoxication, a well known global disease comparable to HPS in ruminants, has been attributed to the steroidal saponin content of this grass. Multiple outbreaks of hepatogenous photosensitisation have been described in sheep, goat and cattle grazing *B. decumbens* (Graydon *et al*., 1991; Smith and Miles, 1993; Lemos *et al*., 1996a; Lemos *et al*., 1996b; Meagher *et al*., 1996; Lemos *et al*., 1997; Lemos *et al*., 1998; Fioravanti, 1999). Because sheep are more susceptible than cattle to lithogenic saponins, intoxication by *Brachiaria* is an important limiting factor for the sheep industry.

Obviously, this grass is not toxic *per se* but certain compounds which as a result of ruminal activities were converted to their derivatives (episarsasapogenin and epismilagenin) responsible for causing toxicity (Noordin, 1988). Diosgenin as {(25*R*)-spirost-5-en-3-B-ol} identified as the major toxic constituent involved in sheep *B. decumbens* intoxication in Malaysia (Zhang, 2000). In addition, recently, a furostanolic steroidal saponin known as 25*R*- e 25*S*- protodioscin isomers in *B. decumbens* leaves was isolated for the first time (Haraguchi *et al*., 2003)

One of the major limitations to efficient ruminant livestock production in Malaysia is the lack of adequate 1evels of high quality forage for feeding to ruminants (Wong *et al*., 1982). Soil acidity a natural phenomenon of most humid tropical grasslands has multiple adverse effects prevails with Al, Mn and Fe toxicity, and P, Ca, Mg, and K deficiency (von Uexküll and Mutert, 1995). Nevertheless, *B. decumbens* is the most widely grown pastures in humid and sub-humid tropics. Apparently, signal grass could provide all the forage requirement of ruminant. It is a stoloniferous, high yielding grass, well adapted to the wide range of soil. Furthermore, *B. decumbens* exhibits high drought resistance and is relatively free from pests and diseases. In Malaysia, this grass has been shown to have an agronomic potential as an excellent pasture species under local climatic condition. It has been extensively planted in all government and smallholding livestock farms since it grows well even with substandard management practices and gives impressive yields of both green and dry matter. Chen and Yuen (1995) reported that improved signal grass pasture was adaptable to a wide range of edaphic and eco-climatic conditions and could support stocking rates from 1,656-2,173 kg/ha of live weight biomass in continuous grazing systems. Consequently, the eradication of this rich grass to avoid its toxicity is rather

impractical, since the available local feed resources in Malaysia were contributed to the poor production performance of small ruminants (Noordin, 1996). Considering the availability and the potent nutritive significance of *B. decumbens*, it is timely aim to find a pragmatic solution to utilize this grass without or with minimal toxic sequel.

To date there is no effective antidote for *B. decumbens* intoxication. Many researches have been done on the prevention of signal grass intoxication with varying degree of success. Therapeutic trials using zinc sulphate, zinc oxide, phenobarbiton and griseofulvin were failed to confer adequate protection. High doses of thiol compounds (like cysteine) can mop-up the toxic metabolites but it is costly and unpractical on apply to livestock.

Depending upon previous studies that had been conducted on the aetiologies, clinical biochemistry and pathophysiology of *B. decumbens* intoxication, studies in this thesis were designed with the following hypothesis.

B. decumbens intoxication can be prevented and treated with vitamin E and selenium administration.

Hence, the reinforcement of antioxidant potential of sheep by using vitamin E and selenium will be significantly maximize which in turn will effectively prevent the development of *B. decumbens* intoxication.

Based on the above hypothesis, the aim of the current studies is to elucidate the efficacy of pre-supplementation of vitamin E and selenium (as prevention) and as a

post supplementation (as treatment) on the development of *B. decumbens* intoxication in sheep in Malaysia with the following objectives:

(¡) to determine the role of oxidoreductive stress in *B. decumbens* intoxication and its suppression by vitamin E and selenium.

(¡¡) to evaluate the efficacy of vitamin E and selenium in alleviating the development of *B. decumbens* intoxication:

a) in intoxicated sheep

b) in preventing intoxication

(¡¡¡) to establish the pathophysiology of hepatotoxicity during *B. decumbens* toxicity in sheep with supplementation of vitamin E and selenium.

REFERENCES

Abas, M.0. and Sharif, H. 1986. Deleterious effects of *Brachiaria decumbens* (Signal grass) on ruminants. *MARDI Report*, 112, 20.

Abas, M.0., Sharif, H., Khusahry, M.Y. and Vance, H.N. 1985. Photosensitisation in goats grazed on *Brachiaria decumbens*. *MARDI Research Bulletin* 13: 203-206.

Abas, M.0., Khusahry, M.Y. and Sheikh Omar, A.R. 1983. Jaundice and photo-sensitisation in indigenous sheep of Malaysia grazing on *Brachiaria decumbens*. *Malaysian Veterinary Journal* 7: 254-263.

Abas, M.0. and Sharif, H. 1988. Hepatotoxicity in indigenous sheep of Malaysia stall-fed with different forms of *Brachiaria decumbens. Pertanika Journal of Tropical Agricultural Science* 11**:** 57-61.

Abdelkader, S.V., Ceh, L., Dishington, I.W. and Hauge, J.G. 1984. Alveld-producing saponins. II. Toxicological studies. *Acta Veterinaria Scandinavica* 25: 76-85.

Allen, R.G. and Balin, A.K. 1989. Oxidative influence on the development and differentiation: An overview of free radical theory of development. *Free Radicals Biology and Medicine* 6: 631-661.

Alvim, M.J., Botrel, M.A., Verneque, R.S. and Salvati, J.A. 1990. Aplicação de nitrogênio emacessos de *Brachiaria* 1. Efeito sobre a produção de matéria seca. *Pasturas Tropicales* 12: 2-6. (Abstract)

Amaral-de-lemos, R.A., Lonzada-Ferreira, L.C., Silva, S.M., Nakazato, L., Salvador, S. and De-Lemos, R.A.A. 1996. Photosensitisation and crystal associated cholangiopathy in sheep grazing *Brachiaria decumbens*. *Ciencia Rural* 26: 109-113.

Anderson, P.H., Berret, S., Catchpoole, J. and Gregory, M.W. 1983. Effect of mon-ensin on the selenium status of sheep. *Veterinary Record* 113: 498-503.

Anderson, R.H. and Anderson, O. 1993. Effects of dietary α-tocopherol and β-carotene on lipid peroxidation induced by methyl mercuric chloride in mice. *Pharmacology and Toxicology* 73: 192-201.

Andreone, P. 2001. Vitamin E as treatment for chronic hepatitis B: results of rando-mized controlled pilot trial. *Antiviral Research* 49: 75-81.

Andres, D. and Cascales, M. 2002. Novel mechanism of vitamin E protection against cyclosporine A cytotoxicity in cultured rat hepatocytes. *Biochemical Pharm-acology* 64: 267-276.

Anon. 1978. Tropical pasture programs. *Ann. Rep.*, pp. 148. Cali., Colombia. CIAT.

Anon. 1979. Tropical pasture programs. *Ann. Rep.*, pp. 113. Cali.; Colombia. CIAT.

Araya, O.S. and Ford, E.J.H. 1981. An investigation of the type of photosensitisation caused by the ingestion of St. John's Wort (*Hypericum perforatum*) by calves. *Journal of Comparative Pathology* 91: 135-141.

Arteel, G.E. 2003. Oxidant and antioxidant in alcohol-induced liver disease. *Gastro-enterology* 124: 778-790.

Assumaidaee, A.A., M. Zamri-Saad, Jasni, S. and M.M. Noordin. 2010. The role of oxidative stress in *Brachiaria decumbens* toxicity in sheep. *Pertanika Journal of Tropical Agricultural Science* 33: 151-157.

Atkinson, H.J. and Babbitt, P.C. 2009. Glutathione S-Transferases are structural and functional outliers in the thioredoxin fold. *Biochemistry* 48: 11108-11116.

Awadeh, F.T., Kincaid, R.L. and Johnson, K.A. 1998. Effect of level and source of dietary selenium on concentrations of thyroid hormones and immuno-globulins in beef cows and calves. *Journal of Animal Science* 76: 1204-1215.

Baber, R. 1989. Photosensitisation: A note of caution in the use of *Brachiaria* pastures-A review. *Tropical Animal Health and Production* 21: 277-280.

Badiei, K., Mostaghni, K., Nazifi, S., Tafti, A.K., Ghane, M. and Momeni, S.A. 2009. Experimental *Panicum miliaceum* poisoning in sheep. *Small Ruminant Research* 82: 99-104.

Bais, H.P., Vepachedu, R., Gilroy, S., Callaway, R.M. and Vivanco, J.M. 2003. Allelopathy and exotic plant invasion: from molecules and genes to species interactions. *Science* 301: 1377-1380.

Bangham, A.D. and Horne, R.W. 1962. Action of saponins on biological cell membranes. *Nature* 196: 952-953.

Barbosa, J.D., Oliveira, C.M.C., Tokarnia, C.H. and Peixoto, P.V. 2006. Hepatic photosensitisation in horses by *Brachiaria humidicola* (Gramineae) in the State of Para. *Pesquisa Veterinária Brasileira* 26: 147-153.

Barry, T.N. and Duncan, S.J. 1984. The role of condensed tannins in nutritional value of *Lotus penduculatus* for sheep. I. Voluntary intake. *British Journal of Nutrition* 51: 485-492.

Basu, S. and Eriksson, M. 2000. Vitamin E in relation to lipid peroxidation in experimental septic shock. *Prostaglandins Leukotrienes and Essential Fatty Acids* 62: 195-199.

Behl, C. 2000. Vitamin E protects neurons against oxidative cell death in vitro more effectively than 17-beta estradiol and induces the activity of the transcription factor NF-kappa B. *Journal of Neural Transmission* 107: 393-407.

Bendich, A. and Machlin, L.J. 1988. Safety of oral intake of vitamin E. *American Journal of Clinical Nutrition* 48: 612-619.

Beutler, E. 1984. *Red cell metabolism: a manual of biochemical methods*. pp.115-116. Grunel and Stratton, Orlando.

Bieri. J.G. 1972. Kinetics of tissue α-tocopberol depletion and repletion. *Annals of the New York Academy of Sciences* 203: 181-191.

Bird, M. 1974. Selenium for weaners. *New Zealand Journal of Experimental Agriculture* 129: 19-23.

Birgel, E.H., Junior, Santos, M.C.D., Ramos, J.A.C. and Benesi, F.J. 2007. Secondary hepatogenous photosensitisation in a llama (*Lama glama*) bred in the state of Sáo Paulo, Brazil. *Canadian Veterinary Journal* 48: 323–324.

Biri, H., Ozturk, H.S. and Buyukkocak, C. 1998. Antioxidant defense potential of rabbit tissues after Eswi: Protective effects of antioxidants vitamin. *Nephron* 79: 181-185.

Bjorneboe, A., Bsjorneboe, G. and Drevon, C. 1990. Absorption, transport and distribution of vitamin E. *Journal of Nutrition* 120: 233–242.

Bjorneboe, A., Nenseter, M., Hagen, B.F., Bjomeboe, G.E., Pryd, C. and Drevon C.A. 1988. Distribution and subcellular localization of alpha-tocopherol in rat liver cells. In: A. Bjorneboe (Ed.), *Transport and Distribution of alpha-tocopherol in Rats*, vol. III, pp. 1-12, Oslo Norway.

Blatt, D.H., Leonard, S.W. and Traber, M.G. 2001. Vitamin E kinetics and the function of tocopherol regulatory proteins. *Nutrition* 17: 799-805.

Blythe, L.L. and Craig, A.M. 1993. Clinical and preclinical diagnostic aids to hepatic plant toxicosis in horses, sheep and cattle. In: Colegate, S.M. and Dorling, P.R. (Eds). *Plant-associated toxins. Agricultural, phyto-chemical and ecological aspects*, pp. 313-318. CAB international.

Bridges, C.H., Camp, B.J., Livingston, C.W. and Bailey, E.M. 1987. Kleingrass (*Panicum coloratum* L.) poisoning in sheep. *Veterinary Pathology* 24: 525-553.

Briton, N.W. and Paltridge, T.B. 1940. Preliminary note on photosensitisation on sheep grazing on *Brachiaria brizantha. Royal Society of Queensland Proceedings* 52: 121-122.

Brown, K.M. and Arthur, J.R. 2001. Selenium, selenoproteins and human health: a review. *Public Health Nutrition* 4: 593-599.

Brum, K.B., Haraguchi, M., Garutti, M.B., Nóbrega, F.N., Rosa, B. and Fioravanti, M.C.S. 2009. Steroidal saponin concentrations in *Brachiaria decumbens* and *B. brizantha* at different developmental stages. *Ciência Rural* 39: 279-281.

Brum, K.B., Haraguchi, M., Lemos, R.A.A. and Fioravanti, M.C.S. 2004. Colangiopatia associada a cristais em ovinos mantidos em pastagem de *Brachiaria decumbens*, In: *Anais do 1º Simpósio Latino-Americano de Plantas Tóxicas*, (*Pesquisa Veterinária Brasileira*, 24, suplemento), 14. (Abstract).

Brum, K.B., Haraguchi, M., Lemos, R.A.A., Riet-Correa, F. and Fioravanti, M.C.S. 2007. Crystal-associated cholangiopathy in sheep grazing *Brachiaria decumbens* containing the saponin protodioscin. *Pesquisa Veterinária Brasileira* 27: 39-42.

Buckmaster, G.W., Cheeke, P.R. and Shull, L.R. 1976. Pyrrolizidine alkaloid poisoning in rats: Protective effects of dietary cysteine. *Journal of Animal Science* 43: 464-473.

Buko, V., Artsukevich, A., Maltsev, A., Nikitin, V., Ignatenko K., Gundermann, K.J. and Schumacher, R. 1994. Effect of polyunsaturated phosphatidylcholine on lipid structure and cAMP-dependent signal transduction in the liver of rats chronically intoxicated with ethanol. *Experimental and Toxicologic Pathology* 46: 375-382.

Buko, V., Sadovnichy, V. 1996. Cytochrome P-450 and free radical generation in rat liver microsomes under the influence of prostaglandin E_2. *Biochemistry and Molecular Biology International* 39: 1177-1184.

Burton, G.W. and Ingold, K.U. 1981. Autooxidation of biological molecules. 1. The antioxidant activity of vitamin E and related chain-breaking phenolic antioxidants in vitro. *Journal of the American Chemical Society* 103: 6472-6477.

Burton, G.W. and Ingold, K.U. 1989. Vitamin E as an *in vitro* and *in vivo* antioxidant. *Annals of the New York Academy of Sciences* 570: 7-22.

Button, C., Paynter, D.I., Shiel, M.J., Colson, A.R., Paterson, P.J. and Lyford, R.L. 1987. Crystal-associated cholangiohepatopathy and photosensitisation in lambs. *Australian Veterinary Journal* 64: 176-180.

Camp, B.J., Bridges, C.H., Hill, D.W., Patamalai, B. and Wilson, S. 1988. Isolation of steroidal sapogenin from the bile of a sheep fed *Agave lecheguilla*. *Veterinary and Human Toxicology* 30: 533-535.

Chang, C.Y., Chen, Y.L., Yang, S.C., Huang, G.C., Tsi, D., Huang, C.C., Chen, J.R. and Li, J.S. 2009. Effect of schisandrin B and sesamin mixture on CCl_4-induced hepatic oxidative stress in rats. *Phytotherapy research* 23: 251-256.

Chang, L.Y., Slot, J.W., Geuze, H.J. and Crapo, J.D. 1988. Molecular immuno-cytochemistry of the Cu/Zn superoxide dismutase in rat hepatocytes. *Journal Cell Biology* 107: 2169-2179.

Cheeke, P.R. 1995. Endogenous toxins and mycotoxins in forage grasses and their effects on livestock. *Journal of Animal Science* 73: 909-918.

Cheeke, P.R. 1996. Biological effects of feed and forage saponins and their impact on animal production. In: W.R. Yamasaki (Ed), *Saponins Used in Food and Agriculture*, pp. 377–385. Plenum Press, New York.

Cheeke, P.R. 1998. Toxins intrinsic to forages. In: Cheeke, P.R. (Ed.), *Natural Toxicants in Feed, Forages and Poisonous Plants*. pp. 275-324. Interstate Publishers, Danville.

Cheeke, P.R., Schmitz, J.A., Lassen, E.D. and Pearson, E.G. 1985. Effects of dietary supplementation with ethoxyquin, magnesium oxide, methionine hydroxy analog and B vitamins on tansy ragwort (*Senecio jacobaea*) toxicosis in beef cattle. *American Journal of Veterinary Research* 46: 2179-2185.

Cheeseman, K.H. and Slater, T.F. 1993. An introduction to free radical biochemistry. *British Medical Bulletin* 49: 481-493.

Chen, C.P. and Yuen, T.K. 1995. *Brachiaria* pastures for animal production in Southeast Asia. *Malaysian Journal of Animal Science* 1: 59-68.

Chen, X. 1986. Selenium and cardiomyopathy (Keshan disease). *Acta pharmacologica et toxicologica* 59: 325-330.

Cheville, N.F. 1983. Cell degeneration. In: N.F. Cheville (Ed), *Cell Pathology*. pp. 75-79, Iowa, U.S.A. Iowa State University Press.

Cheville, N.F. 1994. Normal cell structure. In: N.F. Cheville (Ed), *Ultrastructural pathology: An introduction to interpretation.* pp. 25-69, Iowa, U.S.A. Iowa State University Press.

Chin, F.Y. 1989. Justification, government policy, measures and strategy for the development of grazing reserves in Peninsular Malaysia. In: *Proc. 1st Meet. of Regional FAO Working Group on Grazing and Feed Resources in S.E. Asia*, Feb. 27-Mar. 3, pp. 77-82. Serdang, Malaysia.

Chio, K.S., Reiss, U., Fletcher, B. and Tappel, A.L. 1969. Peroxidation of subcellular organelles: formation of lipofuscin-like fluorescent pigments. Science 166: 1535-1536.

Chow, C.K. 1985. Vitamin E and blood. *World Review of Nutrition Dietetics* 45: 133-166.

Chow, C.K. and Hong, C.B. 2002. Dietary vitamin E and selenium and toxicity of nitrite and nitrate. *Toxicology* 180: 195–207.

Chow, C.K., Ibrahim, W., Wei, Z. and Chan, A.C. 1999. Vitamin E regulates mitochondrial hydrogen peroxide generation. *Free Radical Biology and. Medicine* 27: 580–587.

Clare, N.T. 1952. Photosensitisation in Diseases of Domestic Animals. Review Series No. 3. (Commonwealth Bur. of Animal Health, Commonwealth Agric. Bur., Farnharn Royal, Bucks, England).

Coetzer, J.A.W., Kellerman, T.S., Sadler, W. and Bath, G.F. 1983. Photosensitivity in South Africa. V. A comparative study of the pathology of the ovine hepatogenous photosensitivity diseases, facial eczema and geeldikkop (*Tribulosis ovis*), with special reference to their pathogenesis. *Onderstepoort Journal of Veterinary Research* 50**:** 59-71.

Cogger, V.C., Muller, M., Fraser, R., McLean, A.J., Khan, J. and Le Couteur, D.G. 2004. The effects of oxidative stress on the liver sieve. *Journal of Hepatology* 41: 370–376.

Comb, G.F. 1997. Selenium and cancer prevention. In: H.A. Garewal (Ed.) *Antioxidants and Disease Prevention.* pp. 97-113. CRC Press, New York.

Cooper, W.C., Bennett, K,G. and Croxton, F.C. 1974. The History, Occurrence and Properties of Selenium. In: R.A. Zingaro and W.C. Cooper (Eds.) *Selenium*, pp. 1-30. Van Nostrand Reinhold, New York.

Cruz, C., Driemeier, D., Pires, V.S. and Schenkel, E.P. 2001. Experimentally induced cholangiopathy by dosing sheep with fractionated extracts from *Brachiaria decumbens. Journal of Veterinary Diagnostic Investigation* 13: 170-172.

Cruz, C., Driemeier, D., Pires, V.S., Colodel, E.M., Taketa, A.T.C. and Schenkel, E.P. 2000. Isolation of steroidal sapogenins implicated in experimentally induced cholangiopathy of sheep grazing *Brachiaria decumbens* in Brazil. *Veterinary and Human Toxicology* 42: 142-145.

Culling, C.F. 1974. Handbook of Histopathological and Histochemical Techniques, 3rd Ed., p. 386, Butterworths.

Cuzzocrea, S., Riley, D.P., Caputi, A.P. and Salvemini, D. 2001. A nonpeptidyl mimic of superoxide dismutase with therapeutic activity in rats. *Pharmacological Reviews* 53: 135-159.

Czernichow, S. and Hercberg, S. 2001. Interventional studies concerning the role of antioxidant vitamins in cardiovascular diseases: a review. *Journal of Nutrition, Health* & *Aging* 5: 188–195.

da Costa, R.F.R., Demarque, K.C., dos Santos, I.F., Verardino, H., Almeida, L.A.M., Amoril, J.G., de Freitas, M.R. and Tortelly, R. 2006. Histological aspects of hepatotoxic lesions in the bovine post mortem exam. *Revista Brasileira de Ciência Vetrinaria* 13: 147-150.

Dai, X., Sun, Y. and Jiang, Z. 2007. Protective effects of vitamin E against oxidative damage induced by $A\beta_{1-40}Cu$ (II) complexes. *Acta Biochimica et Biophysica Sinica.* 39: 123–130.

Desjardings, C.G., Beaudet, A., Schipper, H.M. and Brawer, J. 1992. Vitamin E protects beta-endorphin neurons from estradiol neurotoxicity. *Endocrinology* 131: 2481-2482.

Dickinson, J.O. and Ball, R.A. 1985. Management of pyrrolizidine alkaloid toxicity. *California Veterinarian* 39: 15-17.

Diplock, A.T. 1981. In: *Selenium in Biology and Medicine,* pp. 303. AVI Publishing, Hartford, CT.

Dougherty, J.J. and Hoekstra, W.G. 1982. Stimulation of lipid peroxidation in vivo by injected selenite and lack of stimulation by selenate. *Proceedings of the Society for Experimental Biology and Medicine* 169: 209–215.

Drabkin, D.L. and Austin, J.M. 1932. Spectrophotometric constants for common hemoglobin derivatives in human, dog and rabbit blood. *Journal of Biological Chemistry* 98: 719-733.

Driemeier, D., Barros, S.S., Peixoto, P.V., Tokarnia, C.H., Döbereiner, J. and Brito, M.F. 1998. Estudo histológico, histoquímico e ultraestrutural de fígados e linfonodos de bovinos com presença de macrófagos espumosos (“foam cells”). *Pesquisa Veterinária Brasileira* 18: 29-34. (Abstract)

Driemeier, D., Colodel, E.M., Seitz, A.L., Barros, S.S. and Cruz, C.E.F. 2002. Study of experimentally induced lesions in sheep by grazing *Brachiaria decumbens*. *Toxicon* 40: 1027-1031.

Driemeier, D., Döbereiner, J., Peixoto, P.V. and Brito, M.F. 1999. Relação entre macrófagos espumosos ("foam cells") no fígado de bovinos e ingestão de *Brachiaria* spp no Brasil. *Pesquisa Veterinária Brasileira* 19: 79-83. (Abstract).

Dunn, J. 1992. Assessment of liver damage and dysfunction. *In Practice* 14: 193-200.

Duthie, G.G., Wahle, K.W.J. and James, W.P.J. 1989. Oxidants, antioxidants and cardiovascular disease. *Nutrition research reviews* 2: 51-62.

Dutta-Roy, A.K. 1993. Purification and partial characterisation of an α-tocopherol-binding protein from rabbit heart cytosol. *Molecular and Cellular Biochemistry* 123: 139–144.

Ellman, G.L. 1959. "Tissue sulfhydryl groups". *Archives of Biochemistry and Biophysics* 82: 70–77.

El-Shenawy, N., El-Salmy, F., Al-Eisa, R.A. and El-Ahmary, B. 2010. Amelioratory effect of vitamin E on organophosphorus insecticide diazinon-induced oxidative stress in mice liver. *Pesticide Biochemistry and Physiology* 96: 101-107.

Ender, F. 1955. Etiological studies on alveld-a disease involving photosensitisation and icterus in lambs. *Nordisk Veterinaer Medicin* 7: 329-377.

Erskine, R.J. 1998. Making mastitis treatment decisions. In: *Proceedings of the British Mastitis Conference,* Stoneleigh Park, Warwickshire, June 1998. pp 9–14. Axient/Institute for Animal Health, Milk Development Council-/Novartis Animal Health

Evans, H.M. and Bishop, K.S. 1922. On the existence of a hitherto unrecognized dietary factor essential for reproduction. *Science* 56: 650-651.

Fabiana, S.S., Javier, H.A., Jose, M.B., Nelson, S., Nelson, M. and Carlos, G. 2006. Chelate-induced phytoextraction of metal polluted soils with *Brachiaria decumbens*. *Chemosphere* 65: 43-50.

Fagliari, J.J., Passipieri, M., Okuda, H.T., Silva, S.L. and Silva, P.C. 2007. Serum protein concentrations, including acute phase proteins, in calves with hepatogenous photosensitisation. *Arquivo Brasileiro de Medicina Veterinária e Zootecnia* 59: 1355-1358.

Fakurazi, S., Hairuszah, I. and Nanthini, U. 2008. *Moringa oleifera* Lam prevents acetaminophen induced liver injury through restoration of glutathione level. *Food and Chemical Toxicology* 46: 2611-2615.

Fariss, M.W. and Zhang, J.G. 2003. Vitamin E therapy in Parkinson's disease. *Toxicology* 189: 129–146.

Fioravanti, M.C.S.1999. Incidência, avaliações clínica, laboratorial e anatomopatológica da intoxicação subclínica por esporidesmina embovinos. Tese de Doutorado em Medicina Veterinária, Faculdade de Medicina Veterinária e Zootecnia, Universidade Estadual Paulista, Botucatu, SP, Brasil. p. 257. (Abstract)

Flaøyen, A. 1993. *Studies on the aetiology and pathology of alveld*. Thesis of PhD, Norwegian College of Veterinary Medicine. Oslo, Norway.

Flaøyen, A. 1996. Do steroidal saponins have a role in hepatogenous photosensitisation of sheep? *Advances in Experimental Medicine and Biology* 405: 395-403.

Flaøyen, A. 2000. Plant-Associated Hepatogenous Photosensitisation Diseases. In: Gaffield, W. Tu, A.T. (Eds.), *Natural and Selected Synthetic Toxins: Biological Implications,* pp. 204-219. ACS Symposium Series 745. American Chemical Society, Washington, DC.

Flaøyen, A. 1992. Alveld-en historisk oversikt fram til 1940 (Alveld-a historical review up to 1940). *Norsk Veterincertidsskrift* 104: 737-742.

Flaøyen, A., Binde, M., Bratberg, B., Djonne, B., Fjolstad, M., Gronstol, H., Hassan, H., Mantle, P.G., Landsverk, T., Schonheit, J. and Tonnesen, M.H. 1995a. Nephrotoxicity of *Narthecium ossifragum* in cattle in Norway. *Veterinary Record* 137: 259-263.

Flaøyen, A., Bratberg, B., Froslie, A. and Gronstol, H. 1995b. Nephrotoxicity and hepatotoxicity in calves apparently caused by experimental feeding with *Narthecium ossifragum. Veterinary Research Communications* 19**:** 63-73.

Flaøyen, A., Borrebaek, B. and Nordstoga, K. 1991a. Glycogen accumulation and histological changes in the livers of lambs with alveld and experimental sporidesmin intoxication. *Veterinary Research Communications* 15: 443-453.

Flaøyen, A., Bratberg, B. and Gronstol, H. 1995c. Nephrotoxicity in lambs apparently caused by experimental feeding with *Narthecium ossifragum. Veterinary Research Communications* 19**:** 75-79.

Flaøyen, A., Bratberg, B., Froslie, A., Gronstol, H., Langseth, W., Mantle, P.G. and Von Krogh, A. 1997. Nephrotoxicity in goats caused by dosing with water extract from the stems of *Narthecium ossifragum. Veterinary Research Communications* 21: 499-506.

Flaøyen, A., Handeland, K., Stuve, G, Ryeng, K.A. and Refsum, T. 1999. Experimental *Narthecium ossifragum* nephrotoxicity in cervids from Norway. *Journal of Wildlife Diseases* 35: 24-30.

Flaøyen, A., Hjorth, T.H., Gronstol, H. and Karlsen, J. 1991b. Failure to induce toxicity in lambs by administering saponins from *Narthecium ossifragum. Veterinary Research Communications* 15: 483-487.

Flaøyen, A. and Wilkins, A.L. 1997. Metabolism of saponins from *Narthecium ossifragum*-a plant implicated in the aetiology of alveld, a hepatogenous photosensitisation of sheep. *Veterinary Research Communications* 21: 335-345.

Flaøyen, A., Gronst, H. and Soli, N.E. 1991c. Treatment of lambs with phenobarb-itone is not effective against alveld under practical conditions in Norway. *Veterinary Research Communications* 15: 459-461.

Fletcher, B.L. and Tappel, A.L. 1973. Protective effects of dietary α-tocopherol in rats exposed to toxic levels of ozone and nitrogen dioxide. *Environmental Research* 6: 165-175.

Flohe, L., Gunzler, W.A. and Schock, H.H. 1973. Glutathione peroxidase: a selenoe-nzyme. *Federation of the European Biochemical Societies* (*FEBS*) *Letters* 32: 132–134.

Flora, S.J. 2007. Role of free radicals and antioxidants in health and disease. *Cellular and Molecular Biol*ogy 53: 1–2.

Franke, K.W. 1934. A new toxicant occurring naturally in certain samples of plant foodstuffs. I. Results obtained in preliminary feeding trials. *Journal of Nutrition* 8: 597-608.

Franki, T., Salobir, J. and Rezar, V. 2008. The effect of vitamin E supplementation on reduction of lymphocyte DNA damage induced by T-2 toxin and deoxynivalenol in weaned pigs. *Animal Feed Science and Technology* 141: 274–286.

Fry, J.M., Smith, G.M., McGrath, M.C., Speijers, E.J. and Allen, J.G. 1993. Plasma and tissue concentrations of α-tocopherol during vitamin E depletion in sheep. *British Journal of Nutrition* 69: 225-232.

Gee, J.M. and Johnson, I.T. 1988. Interaction between haemolytic saponins, bile, salts and small intestinal mucosa in rat. *Journal of Nutrition* 118: 1391-1397.

Geetha, A., Sankar, R., Marar, T. and Davi, C.S. 1990. Alpha tocopherol reduces doxorubicin idnuced toxicity in rats-histological and biochemical evidences. *Indian Journal of Physiology and Pharmacology* 37: 94-100.

Ghosh, A. and Sil, P.C. 2008. A protein from *Cajanus indicus* Spreng protects liver and kidney against mercuric chloride-induced oxidative stress. *Biological and Pharmaceutical Bulletin* 31: 1651–1658.

Glastonbury, J.R.W., Doughty, F.R., Whitaker, S.J. and Sergeant, E. 1984. A syndrome of hepatogenous photosensitization, resembling geldikkop, in sheep grazing *Tribulus terrestris. Australian Veterinary Journal* 61: 314-316.

Gohl, B. 1981. Tropical Feeds-Feed Information Summaries and Nutritive Values. pp. 174-175. FAO, Rome.

Gokcimen, A., Cim, A., Tola, H.T., Bayram, D., Kocak, A., Ozgüner, F. and Ayata, A. 2007. Protective effect of N-acetylcysteine, caffeic acid and vitamin E on doxorubicin hepatotoxicity. *Human and Experimental Toxicology* 26: 519-525.

Gomar, M.S., Driemeier, D., Colodel, E.M. and Gimeno, E.J. 2005. Lectin histochemistry of foam cells in tissues of cattle grazing *Brachiaria* spp. *Journal of Veterinary Medicine* 52: 18–21.

Gopinath, C. and Ford, E.J.H. 1972. Location of liver injury and extent of bilirubinaemia in experimental liver lesions. *Veterinary Pathology* 9: 99-108.

Grace, N.D. and Lee, J. 1990. Effect of Co, Cu, Fe, Mn, Mo, Se, and Zn supplementation on the elemental content of soft tissues and bone in sheep grazing ryegrass/white clover pasture. *New Zealand Journal of Agricultural Research* 33: 635-647.

Graydon, R.J., Hamid, H., Zaha, R.I.P. and Gardiner, C. 1991. Photosensitisation and crystal-associated cholangiohepatopathy in sheep grazing *Brachiaria decumbens*. *Australian Veterinary Journal* 68: 234-236.

Gregus, Z., Watkins, J.B., Thompson, T.N. and Klassen, C.D. 1982. Resistance of some phase II biotransformation pathways to hepatotoxins. *Journal of Pharmacology and Experimental Therapeutics* 222: 471-479.

Gumpricht, E., Devereaux, M.W., Traber, M. and Sokol, R.J. 2004. Enrichment of rat hepatic organelles by vitamin E administered subcutaneously. *Free Radical Biology and Medicine* 37: 1712–1717.

Habig, W.H., Pabst, M.J. and Jakoby, W.B. 1974. Glutathione S-transferase. The first enzymatic step in mercapturic acid formation. *Journal of Biological Chemistry* 249: 7140–7147.

Halliwell, B. 1997. Antioxidants and human diseases: a general introduction. *Nutrition Reviews* 55: 44-52.

Halliwell, B. and Gutteridge, J.M.C. 1999. Free Radicals in Biology and Medicine, third ed. p. 105. Oxford University Press, Oxford.

Haraguchi, M., Cunha, H.A., Mimaki, Y., Brum, K.B., Lemos, R.A.A., Yokosuka, A. and Sashida, Y. 2003. Furostanol glicosídicos nas folhas de *Brachiaria decumbens*. 26ª Reun. Anu. Soc. Bras. Química, Poços de Caldas, MG. PN-066. (Abstract)

Hasiah, A.H. 2000. *Effect of phenobarbitone and griseofulvin against signal grass* (*Brachiaria decumbens*) *toxicity in sheep*. Thesis of MSc, Universiti Putra Malaysia.

Hayes, J.D. and Pulford, D.J. 1995. The glutathione S-transferase supergene family: regulation of GST and the contribution of the isoenzymes to cancer chemoprotection and drug resistance. *Critical Reviews in Biochemistry and Molecular Biology* 30: 445-600.

Henrici, M. 1952. Comparative study of the content of starch and sugars in *Tribulus terrestris*, lucerne, some Graminae and Pentzia incanum under different meteorological, edaphic and physiological conditions. 2. Carbohydrate nutrition. *Onderstepoort Journal of Veterinary Research* 25: 45-92.

Hill, K.E. 1994. Selenium status and glutathione metabolism. In: R.F. Burk, (Ed.) *Selenium in Biology and Human Health*, pp. 165-166. Springer-Verlag, New York.

Hoffer, A. and Roy. R.M. 1975. Vitamin E decreases erythrocyte fragility after whole-body irradiation. *Radiation Research* 61: 439-443.

Holland, P.T., Miles, C.O., Mortimer, P.H., Wilkins, A.L., Hawkes, A.D. and Smith, B.L. 1991. Isolation of the steroidal sapogenin epismilagenin from the bile of sheep affected by *Panicum dichotomiflorum* toxicosis. *Journal of Agricultural and Food Chemistry* 39: 1963-1965.

Izzo, A.A., Di Carloa, G., Borrellia, F. and Ernstb, E. 2005. Cardiovascular pharmacotherapy and herbal medicines: the risk of drug interaction. *International Journal of Cardiology* 98: 1-14.

Jaeschke, H., Kleinwaechter, C. and Wendel, A. 1992. NADH-dependent reductive stress and ferritin-bound iron in allyl alcohol-induced lipid peroxidation *in vivo*: the protective effect of vitamin E. *Chemico-Biological Interactions* 81: 57-68.

Jenkinson, S.G., Lawrence, R.A., Burk, R.F. and Gregory, P.E. 1983. Non-Se dependent glutathione peroxidase activity in rat lung: association with lung glutathione S- transferase activity and the effects of hyperoxia. *Toxicology and Applied Pharmacology* 68: 399-404.

Johnson, A.E. and Molyneux, R.J. 1984. Toxicity of threadleaf groundsel (*Senecio douglasii var. longilobus*) to cattle. *American Journal of Veterinary Research* 45: 26-31

Johnson, A.E., Molyneux, R.J. and Stuart, L.D. 1985. Toxicity of Ridddell's groundsel (*Senecio riddellii*) to cattle. *American Journal of Veterinary Research* 46: 577-582.

Jones, D.P. 2006. Redefining oxidative stress. *Antioxidants & Redox Signaling* 8: 1865-1879.

Jones, R.J. and Megarrity, R.G. 1983. Comparative toxicity responses of goats fed on *Leucaena leucocephalu* in Australian and Hawaii. *Australian Journal of Agricultural Research* 34: 781-790.

Kagan, V.E. and Quinn, P.J. 1988. The interaction of alpha-tocopherol and homologues with shorter hydrocarbon chains with phospholipid bilayer dispersions. A fluorescence probe study. *European Journal of Biochemistry* 171: 661-667.

Kakkar, P., Das, B. and Vishwanathan, P.N. 1983. A modified spectrophotometric assay of superoxide dismutase. *Indian Journal of Biochemistry and Biophysics* 21: 130-132.

Kalaiselvi, P., Pragasam, V., Chinnikrishnan, S., Veena, C.K., Sundarapandiyan, R. and Varalakshmi, P. 2005. Counteracting adriamycin-induced oxidative stress by administration of N-acetyl cysteine and vitamin E. *Clinical Chemistry and Laboratory Medicine* 243: 834-840.

Kalender, S., Ogutcu, A., Uzunhisarcikli, M., Acikgoz, F., Durak, D., Ulusoy, Y. and Kalender, Y. 2005. Diazinon-induced hepatotoxicity and protective effect of Vitamin E on some biochemical indices and ultrastructural changes. *Toxicology* 211: 197–206.

Kaneko, J.J. 1989. *Clinical Biochemistry of Domestic Animals*. Academic Press, New York.

Kaplowitz, N. 1980. Physiological significance of glutathione S-transferases. *American Journal of Physiology* 239: 439-444.

Kaplowitz, N. and Tsukamoto, K. 1996. Oxidative stress and liver disease. *Progress in Liver Diseases* 14: 131–159.

Keller-Grein, G. Maass, B.L. and Hanson, J. 1996. Natural variation in *Brachiaria* and existing germplasm collections. *In*: J.W. Miles, B.L. Maass and C.B. do Valle (Eds.). *Brachiaria: Biology, agronomy and improvement.* pp. 16-42. CIAT, Cali, Colombia, and CNPGC/EMBRAPA, Campo Grande, MS, Brazil.

Kellerman, T.S. and Coctzer, J.A.W. 1984. Hepatogenous photosensitivity diseases in South Africa (Veterinary Research Institute, Onderstepoort, Technical Communication 193).

Kellerman, T.S., Coetzer, J.A.W., Schnneider, D.J. and Welman, W.G. 1983. Photosensitivity in South Africa.III. Ovine hepatogenous photo-sensitivity caused by the plant *Athanasia trifurcata* L (Asteraceae). *Onderstepoort Journal of Veterinary Research* 50: 45-53.

Kellerman, T.S., Erasmus, G.L., Coetzer, J.A.W., Brown, J.M.M. and Maartens, B.P. 1991. Photosensitivity in South Africa. VI. The experimental induction of geeldikkop in sheep with crude steroidal saponins from *Tribulus terrestris*. *Onderstepoort Journal of Veterinary Research* 58: 47-53.

Kellerman, T.S., Van der Westhuizen, G.C.A., Coetzer, J.A.W., Cecilia, R., Marasas, W.F.O., Minne, J.A., Bath, G.F. and Basson, P.A. 1980. Photosensitivity in Souuth Africa.11. The experimental production of the ovine hepatogenous photosensitivity disease Geeldikop (*Tribulosis ovis*) by the simultaneous ingestion of *Tribulus terrestris* plants and cultures of *Pithomyces chartarum* contain the mycotoxin sporidesmin. *Onderstepoort Journal of Veterinary Research* 47: 231-261.

Kelly, W.R. 1985. The liver and biliary system. In: Jubb, J.V.F., Kennedy, P.C. and Plamer, N. (Eds). *Pathology of domestic animals.* 3rd ed, pp. 302, Orlando, Academic Press.

Khairi, H.M. 2003. *Toxic effects of signal grass* (*Brachiaria decumbens*) *on drug metabolizing enzyme activities in sheep*. Thesis of MSc, Universiti Putra Malaysia.

Kim, J. and Lee, S. 2006. Vitamins C and E protect hepatic cytochrome P-450 dysfunction induced by polymicrobial sepsis. *European Journal of Pharmacology* 534: 202-209.

Klatte, E.T., Scharrer, D.W. and Nagaraja, H.N. 2003. Combination therapy of donepezil and vitamin E in Alzheimer disease. *Alzheimer Disease and Associated Disorders* 17: 113-116.

Klingenberg, M. 1958. Pigment of rat liver microsomes. *Archives of Biochemistry and Biophysics* 75: 376-386.

Kosower, N.S. and Kosower, E.M. 1978. The Glutathione status of cells. *International Review of Cytology* 54: 109-156.

Lacaille-Dubois, M.A. and Wagner, H. 2000. Bioactive saponins from plants: An update. *Studies in Natural Products Chemistry* 21: 633-687.

Lajis, N.H., Abdullah, S.A., Salim, J.S., Bremmer, J.B. and Khan, M.N. 1993. Epi-sarsasapogenin and epi-smilagenin isolated from the rumen content of sheep intoxicated by *Brachiaria decumbens*. *Steroids* 58: 387-389.

Lancaster, M.J., Vit, I. and Lyford, R.L. 1991. Analysis of bile crystals from sheep grazing *Panicum schinzii* (sweet grass). *Australian Veterinary Journal* 68: 281-288.

Landes, N., Pfluger, P., Kluth, D., Birringer, M., Ruhl, R., Bol, G.F., Glatt, H. and Brigelius-Flohe, R. 2003. Vitamin E activates gene expression via the pregnane X receptor. *Biochemical Pharmacology* 65: 269-273.

Langseth, W., Torgersen, T., Kolsaker, P., Romming, C., Jantsch, T.G., Mantle, P.G., Pearce, J., Gibson, S.E. Goicochea, M.G. and Flaoyen, A. 1999. Isolation and characterization of 3-methoxy-2(5H)-furanone as the principal nephrotoxin from *Narthecium ossifragum* (L.). Huds. *Natural Toxins* 7: 111–118.

Larsen, H.J., Moksnes, K. and Overnes, G. 1988. Influence of selenium on antibody production in sheep. *Research in Veterinary Science* 45: 4-10.

Laskin, D.L., Robertson, F.M., Pilaro, A.M. and Laskin, J.D. 2005. Activation of liver macrophages following phenobarbital treatment of rats. *Hepatology* 8: 1051-1055.

Lawrence, R.A. and Burk, R.F. 1976. Glutathione peroxidase activity in selenium-deficient rat liver. *Biochemical and Biophysical Research Communications* 71: 952-958.

Lemos, R.A.A. and Leal, C.R.B. 2008. *Economic impact of diseases in beef cattle: Questions and Answers*. pp. 232-236. UFMS, Campo Grande.

Lemos, R.A.A., Osório, A.L.A.R., Rangel, J.M.R. and Herrero Junior, G.O. 1996a. Fotossensibilização e colangiopatia associada a cristais em bezerros ingerindo *Brachiaria brizantha*. *Arqs Inst. Biológico São Paulo* 63: 22. (Abstract)

Lemos, R.A.A., Ferreira, L.C.L., Silva, S.M., Nakazato, L. and Salvador, S.C. 1996b. Fotossensibilização e colangiopatia associada a cristais em ovinos em pastagem com *Brachiaria decumbens*. *Ciência Rural, Santa Maria* 26: 109-113. (Abstract)

Lemos, R.A.A., Salvador, S.C. and Nakazato, L. 1997. Photosensitisation and crystal associated cholangiohepatopathy in catlle grazing *Brachiaria decumbens* in Brazil. *Veterinary and Human Toxicology* 39: 376-377.

Lemos, R.A.A., Nakazato, L., Herrero Junior, G.O., Silveira, A.C. and Porfírio, L.C. 1998. Fotossensibilização e colangiopatia associada a cristais em caprinos mantidos sob pastagens de *Brachiaria decumbens* no Mato Grosso do Sul. *Ciência Rural* 28: 507-510. (Abstract)

Lennon. S., Martin, S. and Cotter, T. 1991. Dose-dependent induction of apoptosis in human tumor cell lines by widely diverging stimuli. *Cell Proliferation* 24: 203-14.

Levander, O.A., Morris, V.C. and Ferretti, R.J. 1975. Lead poisoning in vitamin E-deficient rats. *Journal of Nutrition* 105: 1481-1485.

Levander, O.A. 2000. The selenium-coxsackie virus connection: Chronicle of a collaboration. *Journal of Nutrition* 130: 4859–4885.

Li, M., Osaki, M., Rao, I.M. and Tadano, T. 1997. Secretion of phytase from the roots of several plant species under phosphorus-deficient conditions. *Plant and Soil* 195: 161-169.

Liu, S.L., Esposti, S.D., Yao, T., Diehl, A.M. and Zern, M.A. 1995.Vitamin E therapy of acute CCl_4-induced hepatic injury in mice is associated with inhibition of nuclear factor kappa B binding. *Hepatology* 22: 1474–1481

Loch, D.S. 1977. *Brachiaria decumbens* (Signal grass) - A review with particular reference to Australia. *Tropical Grasslands* 11: 141-157.

Lukivskaya, O., Zavodnik, L., Knas, M. and Buko, M. 2006. Antioxidant mechanism of hepatoprotection by ursodeoxycholic acid in experimental alcoholic steatohepatitis. *Advances in Medical Sciences* 51: 54-59.

Luna, L.G. 1968. Manual of Histologic Staining Methods of The Armed Forces Institute of Pathology, 3rd ed., pp. 38-39. McGraw-Hill, New York.

Macedo, M.C.M. 2005. Pastagens no Ecossitema Cerrados: evolução das pesquisas para o desenvolvimento sustentável. Anais 42ª Reun. Anu. Soc. Bras. *Zootecnia, Goiânia*, pp. 56-84. (Abstract)

Macfarlane, D. and Shelton, H.M. 1986. "Pasture in Vanuatu". ACIAR Technical Report 2.

Malone, F.E., Kennedy, S., Reilly, G.A.C. and Woods, F.M. 1992. Bog asphodel (*Narthecium ossifragum*) poisoning in cattle. *Veterinary Record* 131: 100-103.

Manor, D. and Morley, S. 2007. The α-tocopherol transfer protein. *Vitamins & Hormones* 76: 45-65.

Marklund, S. and Marklund, G. 1974. Involvement of the superoxide anion radical in the autoxidation of pyrogallol and a convenient assay for superoxide dismutase. *European Journal of Biochemistry* 47: 469-474.

Maros, T.N., Fodor, G.P., Virginia, V., Kovacs, V.V. and Katonai, B. 1990. Effect of selenium and vitamin E on the regeneration of rat liver. *Journal of Nutrition* 90: 219-227.

Maruyama, H. and Listowsky, I. 1984. Preferential binding of steroids by anionic forms of rat glutathione S-transferase. *Journal of Biological Chemistry* 20: 12449-12455.

Masukawa, T., Nishimura, T. and Iwata, H.1984. Differential changes of glutathione S-transferase activity by dietary selenium. *Biochemical Pharmacology* 33: 2635-2639.

Mathews, F.P. 1937. Lechuguilla (*Agave lecheguilla*) poisoning in sheep, goats and laboratory animals. *Texas Agricultural Experiment Station Bulletin*, No. 554, pp. 36.

Mathews, F.P. 1938a. Lechuguilla (*Agave lecheguilla*) poisoning in sheep and goats. *Journal of the American Veterinary Medical Association* 93: 168-175.

Mathews, F.P. 1938b. An experimental investigation of *Lecheguilla* poisoning. *Archives of Pathology* 25: 661-683.

Mathews, F.P. 1940. Poisoning of sheep and goats by sacahuiste (*Nolina texana*) buds and blooms. *Texas Agricultural Experiment Station Bulletin*. No. 585, pp. 19.

Mazel, P. 1971. General principles and procedures for drug metabolism in vitro. In: B.N.Du, H.G. Mandel, and E.L. Way (Eds), *Fundamentals of Drug Metabolism and Disposition*, pp. 527-541.Williams and Wilkins, Baltimore.

McCay, P.B. 1985. Vitamin E: Interactions with free radicals and ascorbate. *Annual Review of Nutrition* 5: 323-340.

McFarlane, D. and Shelton, H.M. 1986. Pastures in Vanuatu. Canberra, ACIAR Technical Report Series No. 2.

McKenzie, R.C., Rafferty, T.S. and Beckett, G.J. 1998. Selenium: an essential element for immune function. *Immunology Today* 19: 342-345.

Meagher, L.P., Miles, C.O. and Fagliari, J.J. 1996. Hepatogenous photosensitisation of ruminants by *Brachiaria decumbens* and *Panicum dichotomiflorum* in the absence of sporidesmin: lithogenic saponins may be responsible. *Veterinary and human toxicology* 38: 271-274.

Medina, J. and Moreno-Otero, R. 2005. Pathophysiological basis for antioxidant therapy in chronic liver disease. *Drugs* 65: 2445-461.

Meeks, R.G., Harrison, S.D. and Bull, R.J. 1991. *Hepatotoxicology*. *CRC* Press,-London.

Meydani, S.N., Meydani, M. and Blumberg, J.B. 1998. Assessment of the safety of supplementation with different amounts of vitamin E in healthy older adults. *American Journal of Clinical Nutrition* 68: 311–318.

Morais, M.G., Rangel, J.M., Madureira, J.S. and Silveira, A.C. 2000. Seasonal changes of clinical biochemistry of graded Nelore cows on continuous grazing of *Brachiaria decumbens*. *Arquivo Brasileiro de Medicina Veterinária e Zootecnia* 52: 98-104.

Milad, K., Racz, O., Sipulova, A., Bajova, V. and Kovac, G. 2001. Effect of vitamin E and selenium on blood glutathione peroxidase activity and some immunological parameters in sheep. *Veterinarni Medicina* 46: 1-5.

Milchak, L.M. and Bricker, J.D. 2002. The effects of glutathione and vitamin E on iron toxicity in isolated rat hepatocytes. *Toxicology Letters* 126: 169-177.

Miles, C.O., Munday, S.C., Holland, P.T, Smith, B.L, Embling, P.P. and Wilkins, A.L. 1991. Identification of a sapogenin glucoronide in the bile of sheep affected by *Panicum dichotomiflorum* toxicosis. *New Zealand Veterinary Journal* 39: 150-152.

Miles, C.O., Munday, S.C., Holland, P.T., Lancaster, M.J. and Wilkins, A.L. 1992a. Further analysis of bile crystals from sheep grazing *Panicum schinzii* (sweet grass). *Australian Veterinary Journal* 69: 34-39.

Miles, C.O., Wilkins, A.L., Munday, S.C., Holland, P.T., Smith, B.L., Lancaster, M.J. and Embling, P.P. 1992b. Identification of the calcium salt of epismilagenin beta-D-glucuronide in the bile crystals of sheep affected by *panicum dichotomiflorum* and *panicum schinzii* toxicoses. *Journal of Agricultural and Food Chemistry* 40: 1606–1609.

Miles, C.O., Wilkins, A.L., Erasmus, G.L., Kellerman, T.S. and Coetzer, J.A.W. 1994a. Photosensitivity in South Africa. VII. Chemical composition of biliary crystals from a sheep with experimentally induced geeldikkop. *Onderstepoort Journal of Veterinary Research* 61: 215-222.

Miles, C.O., Wilkins, A.L., Erasmus, G.L. and Kellerman, T.S. 1994b. Photosensitivity in South Africa. VIII. Ovine metabolism of *Tribulus terrestris* saponins during experimentally induced geeldikkop. *Onderstepoort Journal of Veterinary Research* 61: 351-359.

Miles, C.O., Wilkins, A.L., Munday, S.C., Flaoyen, A., Holland, P.T.and Smith, B.L. 1993. Identification of insoluble salts of the ß-D-glucuronides of epi-sarsasapogenin and epi-smilagenin in the bile of lambs with alveld and examination of *Narthecium ossifragum*, *Tribulus terrestris* and *Panicum miliaceum* for sapogenins. *Journal of Agricultural and Food Chemistry* 41: 914-917.

Miles, J.W. and do Valle, C.B. 1996. Manipulation of apomixis in *Brachiaria* breeding. In: J.W. Miles, B.L. Maass and C.B. do Valle (Eds.). *Brachiaria: biology, agronomy and improvement*. pp. 164-177. CIAT: Cali, Colombia and CNPGC/EMBRAPA: Campo Grande, MS, Brazil.

Mills, G.C. 1957. Hemoglobin catabolism. I. Glutathione peroxidase, an erythrocyte enzyme which protects hemoglobin from oxidative breakdown. *Journal of Biological Chemistry* 229: 189-197.

Milner, L.S., Wei, S.H., Stohs, S.J., Eldeen, Z.M. and Houser, M.T. 1992. Role of glutathione metabolism in the reduction of proteinuria by dimethylthiourea in adriamycin nephrosis. *Nephron* 62: 192-197.

Miranda, C.H.B. and Boddey, R.M. 1987. Estimation of biological nitrogen fixation associated with 11 ecotypes of *Panicum maximum* grown in nitrogen-15-labeled soil. *Agronomy Journal* 79: 958-963.

Miranda, C.L., Reed, R.L., Cheeke, P.R. and Buhler, D.R. 1981. Protective effects of butylated hydroxyanisole against the acute toxicity of monocrotaline in mice. *Toxicology and Applied Pharmacology* 59: 424-430.

Mitchell, J.R., Hinson, J.A. and Nelson, S.D. 1976. Glutathione and drug-induced tissue lesions. In: Arias, I.M., Jakoby, W.B. (Eds.), *Glutathione: Metabolism and Function*, pp. 357–367. Raven Press, New York.

Moksnes, K. and Gunnar, N. 1983. Selenium and glutathione peroxidase levels in lambs receiving feed supplemented with sodium selenite or seleno-methionine. *Acta Veterinaria Scandinavica* 24: 45-58.

Morais, M.G., Rangel, J.M., Madureira, J.S. and Silveira, A.C. 2000. Seasonal changes of clinical biochemistry of graded Nelore cows on continuous grazing of *Brachiaria decumbens. Arquivo Brasileiro de Medicina Veterinária e Zootecnia* 52: 98-104.

Muchiri, D.J., Bridges, C.H., Ueckert, D.N. and Bailey, E.M. 1980. Photosensitisation of sheep on kleingrass pasture. *Journal of the American Veterinary Medical Association* 177: 353-354.

Mukherjee, R. 2008. Selenium and vitamin E increases polymorphonuclear cell phagocytosis and antioxidant levels during acute mastitis in riverine buffaloes. *Veterinary Research Communications* 32: 305-313.

Mullenax, C.H. 1991. *Brachiaria decumbens* toxicity-grass or fungus. A letter to the editor. *Veterinary and Human Toxicology* 33: 464-465.

Munday, S.C., Wilkins, A.L., Miles, C.O. and Holland, P.T. 1993. Isolation and structure elucidation of dichotomin, a furostanol saponin implicated in the hepatogenous photosensitisation of sheep grazing on *panicum dichotomiflorum*. *Journal of Agricultural and Food Chemistry* 41**:** 267-271.

Murdiati, T.B. and Lowry, J.B. 1983. *Toxicity of B. decumbens*. Research report. Project for animal research and development. pp. 56-57, Ciawi, Indonesia.

Murdiati, T.B., McSweeney, C.S., Campble, R.S.F. and Stoltz, D.S. 1990. Prevention of hydrolyzable tannin toxicity in goats fed *Clidema hitiu* by calcium hydroxide supplementation. *Journal of Applied Toxicology* 10: 325-331.

Muriel, P. and Suarez, O.R. 1994. Role of lipid peroxidation in biliary obstruction in the rat. *Journal of Applied Toxicology* 14: 423-426.

Murry, M. 1991. In vitro and in vivo studies of the effect of vitamin E on microsomal cytochrome P-450 in rat liver. *Biochemical Pharmacology* 42: 2107-2114.

Mustacich, D.J., Bruno, R.S. and Traber, M.G. 2007. Vitamin E. *Vitamins & Hormones* 76: 1-21.

Navarro-Alarcon, M. and Cabrera-Vique, C. 2008. Selenium in food and the human body: A review. *Science of the Total Environment* 400: 115-141.

Navarro-Alarcón, M., López-G, H., Serrana, D.L., Pérez-Valero, V. and López Martínez, M.C. 2002. Selenium concentrations in serum of individuals with liver diseases (cirrhosis or hepatitis): relationship with some nutritional and biochemical markers. *Science of the Total Environment* 291: 135-141.

Nielsen, F., Mikkelsen, B., Nielsen, J.P., Andersen, H.R. and Grandjean, P. 1997. Plasma malondialdehyde as biomarker for oxidative stress: reference interval and effects of life-style factors. *Clinical Chemistry Journal* 43: 1209-1214.

Niki, E., Yamamoto, Y., Takahashi, M., Komuro, E. and Miyama, Y. 1989. Inhibition of oxidation of biomembranes by tocopherol. *Annals of the New York Academy of Sciences* 570: 23-31.

Nishikmi, M., Rao, N.A. and Yagi, K. 1972. The occurrence of superoxide anion in the reaction of reduced phenazine metosulfate and molecular oxygen. *Biochemical and Biophysical Research Communications* 46: 849-854.

Njeru, C.A., McDowell, L.R., Wilkinson, N.S., Linda, S.B., Rojas, L.X. and Williams, S.N. 1994. Serum and tissue tocopherol in sheep after intramuscular injection and (or) dietary vitamin E supplementation. *Journal of Animal Science* 72: 739-745.

Nobre, D. and Andrade, S.O. 1976. Relationship between photosensitisation in young cattle and *Brachiaria decumbens* Stapf. *Biológico São Paulo* 42: 249-258.

Noordin, M.M. 1988. *The toxicity of Brachiaria decumbens*. Thesis of MSc, Universiti Putra Malaysia.

Noordin, M.M. 1996. Trace element research in sheep in Malaysia. The Australian Centre for International Agricultural Research (ACIAR) Proceedings 73: 72-77.

Noordin, M.M., Salam Abdullah, A. and Rajion, M.A. 1989. Experimental *Brachiaria decumbens* toxicity in cattle. *Veterinary Research Communications* 13: 491–494.

Noordin, M.M., Shokri, J. and Sheikh-Omar, A.R. 1999. Nutritional muscular degeneration in cattle in Malaysia: report of two cases. *Journal Veterinar Malaysia* 11: 99-102.

Noordin, M.M., Zamri-Saad, M., Salam Abdullah, A. and Rajion, M.A. 1987. Effects of grazing of *B. decumbens* on the ultrastructure of liver and kidney of sheep. *Kajian Veterinar* 19: 215-218.

Norenberg, M.D., Jayakumar, A.R. and Rama Rao, K.V. 2004. Oxidative stress in the pathogenesis of hepatic encephalopathy. *Metabolic Brain Disease* 19: 313-329.

Obersteiner, E.J. and Sharma, R.P. 1978. Effect of vitamin E on selenium cytotoxicity in chick ganglia cultures. *Toxicology* 9: 165-172.

Ohkawa, H., Ohishi, N. and Yagi, K. 1979. Assay for lipid peroxides in animal tissues by thiobarbituric acid reaction. *Analytical Biochemistry* 95: 351-358.

Oleszek, W.A. 2002. Chromatographic determination of plant saponins. *Journal of Chromatography* 967: 147-162.

Oliveira, G.P., Nbvaes, A.P. and Costa, A.J. 1979. Photosensitivity in sheep caused by *Pithomyces chartarum* in a *Brachiaria decumbens* pasture in the Sao Carios region in Sao Paulo State. *Cientifica* 7: 17-22.

Omura, T. and Sato, R. 1964. The carbon monoxide-binding pigment of liver microsomes. *Journal of Biological Chemistry* 239: 2370-2378.

Onyema, O.O., Farombi, E.O., Emerole, G.O., Ukoha, A.I. and Onyeze, G.O .2006. Effect of vitamin E on monosodium glutamate induced hepatotoxicity and oxidative stress in rats. *Indian Journal of Biochemistry and Biophysics* 43: 20-24.

Opasina, B.A. 1985. Photosensitisation jaundice syndrome in West African dwarf sheep and goats grazed on *Brachiaria decumbens*. *Tropical Grasslands* 19: 120-123.

Orrenius, S., Gogvadze, V. and Zhivotovsky, B. 2007. Mitochondrial oxidative stress: implications for cell death. *Annual Review of Pharmacology and Toxicology* 47: 143-183.

Ortolani, E.L. 2001. Sulpher deficiency in dairy calves reared on pasture of *Brachiaria decumbens. Ciência Rural Santa Maria* 31: 257-261.

Othman, A.M.; Haron, S.; Yusuff, M.K. and Saad, M.Z. 1983. Hepatogenous photosensitivity in Indigenous sheep of Malaysia grazing on pure stand of leafy regrowth of *Brachiaria decumbens. Malaysian Veterinary Journal* 7: 271-273.

Paglia, D.E. and Valentine, W.N. 1967. Studies on the quantitative and qualitative characteristics of erythrocyte glutathione peroxidase. *Journal of Laboratory and Clinical Medicine* 70: 158-169.

Panozzo, P.M., Basso, D., Balint, L., Biasin, M.R., Bonvicini, P. and Metus, P. 1995. Altered lipid peroxidation/glutathione ratio in experimental extrahepatic cholestasis. *Clinical and Experimental Pharmacology and Physiology* 22: 266-271.

Pascoe, G.A., Olafsdottir, K. and Reed, D.J. 1987. Vitamin E protection against chemical-induced cell injury. I. Maintenance of cellular protein thiols as a cytoprotective mechanism. *Archives of Biochemistry and Biophysics* 256: 150-158.

Pass, M.A. 2008. Current ideas on the pathophysiology and treatment of *lantana* poisoning of ruminants. *Australian Veterinary Journal* 63: 169-171.

Paulino, V.T. Anton, D.P. and Colozza, M.T. 1987. Problemas nutricionais do género *Brachiaria* e algumas relações com o comportamento animal. *Zootecnia* 25: 215-263. (Abstract)

Pearson, E.G. and Craig, A.M. 1980. The diagnosis of liver diseases in equine and food animals. Part two: Evaluation of liver damage and functional failure. *Modern Veterinary Practice* 61: 315-320.

Pérez, M.J. and Cederbaum, A.I. 2003. Adenovirus-mediated expression of Cu/Zn - or Mn superoxide dismutase protects against CYP2E. *Hepatology* 38: 1146-1158.

Persson-Moschos, M., Huang, W., Srikumar, T.S. and Akesson, B. 1995. Seleno-protein P in plasma as a biochemical marker of selenium status. *Analyst* 120: 838-836.

Pires, V.S., Taketa, A.T.C., Gosmanna, G. and Schenkel, E.P. 2002. Saponins and sapogenins from *Brachiaria decumbens* stapf. *Journal of the Brazilian Chemical Society* 13: 135-139.

Pompella, A. and Comporti, M. 1993. Imaging of oxidative stress at subcellular levels by confocal laser scanning microscope after fluorescent derivativization of cellular carbonyls. *American Journal of Pathology* 142: 1353-1359.

Powers, S.K. and Jackson, M.J. 2007. Exercise-induced oxidative stress: cellular mechanisms and impact on muscle force production. *Physiological Reviews* 88: 1243-1276.

Price, K.R., Johnson, I.T. and Fenwick, G.R. 1987. The chemistry and biological significance of saponins in foods and feeding stuffs. *CRC Critical Reviews in Food Science and Nutrition* 26: 27-135.

Pruijn, F.B., Haenen, G.R.M.M. and Bast, A. 1991 Interplay between vitamin E, glutathione and dihydrolipoic acid in protection against lipid peroxidation. *Fat Science Technology* 6: 216-221.

Quinn, P.J. 2007. Molecular associations of vitamin E. *Vitamins & Hormones* 76: 67-98.

Rankins, D.L., Smiths, G.S., Ross, T.T., Caton, J.S. and Kloppenburgs, P. 1993. Characterization of toxicosis in sheep dosed with Blossoms of Sacahuiste (*Nolina microcarpa*). *Journal of Animal Science* 71: 2489-2498.

Rao, I.M., Kerridge, P.C. and Macedo, M. 1996. Nutritional requirements of *Brachiaria* and adaptation to acid soils. In: J.W. Miles, B.L. Maass and C.B. do Valle (Eds.). *Brachiaria: biology, agronomy, and improvement*. pp. 53-71. CIAT: Cali, Colombia and CNPGC/EMBRAPA: Campo Grande, MS, Brazil.

Rao, I.M., Miles, J.W. and Granobles, J.C. 1998. Differences in tolerance to infertile acid soil stress among germplasm accessions and genetic recombinants of the tropical forage grass genus, *Brachiaria*. *Field Crops Research* 59: 43-52.

Ray, S.D. and Fariss, M.W. 1994. Role of cellular energy status in tocopheryl hemisuccinate cytoprotection against ethyl methanesulfonate-induced toxicity. *Archives of Biochemistry and Biophysics* 311: 180-190.

Reed, D.J., Pascoe, G.A. and Olafsdottir, K. 1987. Some aspects of cell defense mechanisms of glutathione and vitamin E during cell injury. *Archives of Toxicology* 11: 34-38.

Reis Junior, F.B., Reis, V.M., Urquiaga, S. and Do bereiner, J. 2000. Influence of nitrogen fertilization on the population of diazotrophic bacteria Herbaspirillum spp. and Acetobacter diazotrophicus in sugarcane (Saccharum spp.). *Plant Soil* 219: 153–159.

Riet-Correa, G., Riet-Correa, F., Schild, A.L. and Driemeier, D. 2002. Wasting and death in cattle associated with chronic grazing of *Brachiaria decumbens*. *Veterinary and Human Toxicology* 44: 179-180.

Ritland, S. and Aaseth, J. 1987. Trace elements and the liver. *Journal of Hepatology* 5: 118–122.

Rogers, Q.R., Knight, H.D. and Gulick, B.A. 1979. Proposed method of diagnosis and treatment of pyrrolizidine alkaloid toxicity in horses. In: P. R. Cheeke (Ed.) *Symposium on Pyrrolizidine* (*Senecio*) *Alkaloids: Toxicity, Metabolism, and Poisonous Plant Control Measures*. pp. 145-147. The Nutrition Research Institute, Oregon State Univ., Corvallis.

Ronis, M.J.J., Butura, A., Sampey, B.P., Prior, R.L., Korourian, S. and Albano, E. 2005. Effects of N-acetyl cysteine on ethanol-induced hepatotoxicity in rats fed via total enteral nutrition. *Free Radical Biology and Medicine* 36: 616–630.

Rotruck, J.T., Pope, A.L., Ganther, H.E., Swanson, A.B., Hafeman, D.G. and Hoekstra, W.G. 1973. Selenium: biochemical role as a component of glutathione peroxidase. *Science* 179: 588–590.

Roy, M., Schumacher, L.K., Wishe, H.I., Cohen, M.W., and Stotzky, G. 1995. Supplementation with selenium restores age-related decline in immune cell function. *Proceedings of the Society for Experimental Biology and Medicine* (*PSEBM*) *Journal* 209: 369-375.

Rungby, J., Ellermann-Eriksen, S. and Danscher, G. 1987. Effects of selenium on toxicity and ultrastructural localization of silver in cultured macrophages. *Archives of Toxicology* 61: 40-45.

Ryter, S.W., Kim, H.P., Hoetzel, A., Park, J.W., Nakahira, K., Wang, X. and Choi, A.M.K. 2007. Mechanisms of cell death in oxidative stress. *Antioxidants and Redox Signaling* 9: 49-89.

Sahin, K., Sahin, N., Onderci, M., Yaralioglu, S. and Kucuk, O. 2001. Protective role of supplemental vitamin E on lipid peroxidation, vitamins E, A and some mineral concentrations of broilers reared under heat stress. *Veterinarni medicina Czech.* 46: 140-144.

Sakamoto, T., Liu, Z., Murase, N., Ezure, T., Yokomuro, S., Poli, V. and Demetris, A.J. 1999. Mitosis and apoptosis in the liver of interleukin-6-deficient mice after partial hepatectomy. *Hepatology* 292: 403-411.

Salam Abdullah, A. 1987. Toxic extract of rumen liquor of sheep fed *Brachiaria decumbens. Proc. IFS symposium of Science Asia, 87*. October 14-17, pp. 83-86. Kuala Lumpur.

Salam Abdullah, A. and Rajion, M.A. 1990. Signal grass (*Brachiaria decumbens*) toxicity in sheep. Changes in rumen microbial populations and volatile fatty acid concentration. *Veterinary and Human Toxicology* 32: 444-445.

Salam Abdullah, A., Noordin, M.M. and Rajion, M.A. 1987. Toxicity of *Brachiaria decumbens* in sheep and goats. *Proceeding 1st Congress of Toxicology in Developing Countries*, November 15-21, Buenos Aires, Argentina.

Salam Abdullah, A., Noordin, M.M. and Rajion, M.A. 1988. Signal grass (*Brachiaria decumbens*) toxicity in sheep: changes in motility and pH of reticulo-rumen. *Veterinary and Human Toxicology* 30: 256-258.

Salam Abdullah, A., Noordin, M.M. and Rajion, M.A. 1989. Neurological disorders in sheep during Signal grass (*Brachiaria decumbens*) toxicity. *Veterinary and Human Toxicology* 31: 128-129.

Salam Abdullah, A., Noordin, M.M., Rajion, M.A., Ragavan, K. and Osman, A. 1994. The use of zinc sulphate for prevention of *B. decumbens* (Signal grass) toxicity in sheep. *Proceedings of the 6th International Congress European Association Veterinary Pharmacology and Toxicology*.7-11 August, p. 121-122. Edinburgh, United Kingdom.

Salam Abdullah, A., Nordin, L., Bremner, J.B., Davies, N.W., Mustapha, W. and Rajion, M.A. 1992. Hepatotoxic constituents in the rumen of *Brachiaria decumbens* intoxicated sheep. *Veterinary and Human Toxicology* 34: 154-155.

Salam Abdullah, A., Rajion, M.A., Zamri-Saad, M. and Yahya, I. 1990. Individual variation in resistance to *Brachiaria decumbens* toxicity in sheep. *Journal Veterinar Malaysia* 2: 135-138.

Sansinanea, A.S., Cerone, S.I., Streitenberger, S.A., Garcia, C. and Auza, N. 1997. Superoxide dismutase activity and reduced glutathione levels in Cu-overload liver from sheep. *Nutrition Research* 17: 115-123.

Santos, E.D.G., Paulino, M.F. and Queiroz, D.S. 2004. Avaliação de pastagem diferida de *Brachiaria decumbens* stapf: características químico-bromatológicas da forragem durante a seca. *Revista Brasileira de Zootecnia* 33: 203-213. (Abstract)

Satoh, K. 1978. Serum lipid peroxide in cerebrovascular disorders determined by new colorimetric method. *Clinica Chimica Acta* 90: 37-43.

Saturnino, A. and Klaus, C. 2010. Experimental poisoning by *Brachiaria decumbens* in feedlot sheep. *Pesquisa Veterinária Brasileira* 30: 195-202.

Sazuka, Y., Tanizawa, H. and Takino, Y. 1989. Effect of adriamycin on the activities of superoxide dismutase, glutathione peroxidase and catalase in tissues of mice. *Japanese Journal of Cancer Research* 80: 89-94.

Scandalios, J.G. 1990. Response of plant antioxidant defense genes to environmental stress. *Advances in Genetics* 28: 1-41.

Scheie, E., Ryste, E.V. and Flaoyen, A. 2003. Measurement of phylloerythrin (phytoporphyrin) in plasma or serum and skin from sheep photosensitised after ingestion of *Narthecium ossifragum*. *New Zealand Veterinary Journal* 51: 99-103.

Schneider, C. 2005. Chemistry and biology of vitamin E. *Molecular Nutrition and Food Research* 49: 7-30.

Schrauzer, G.N. 1994. Selenium in the maintenance and therapy of HIV-infected patients. *Chemico-biological Interactions* 91: 199-205.

Seawright, A.A. 1982. Animal health in Australia, vol. 2, *Chemical and plant poisons*, pp. 27-106, Australian Government Publishing Service, Canberra.

Sedlak, J. and Lindsay, R. 1968. Estimation of total, protein-bound, and nonprotein-sulfhydryl groups in tissue with Ellman's reagent. *Analytical Biochemistry* 25: 195-200.

Seitz, A.L., Rozza, D.B., Feltrin, C., Traverso, S.D., Colodel, E.M. and Driemeier, D. 2004. Fotossensibilização por *Brachiaria decumbens* em ovinos no Rio Grande do Sul. *Pesquisa Veterinária Brasileira* 24: 67-69. (Abstract)

Sen, C.K., Roy, S. and Packer, L. 1998. Oxidants and antioxidants in glutamate-induced cytotoxicity. In: Packer, L., Ong, A.S.H. (Eds.), *Biological Oxidants and Antioxidants*, pp. 5–13. AOCS Press, Champaign.

Sen, S., Makkar, H.P.S., Muetzel, S. and Becker, K. 1998. Effect *of Quillaja saponaria* and *Yucca schidigera* plant extract on growth of *Escherichia coli*. *Letters in Applied Microbiology* 27: 35–38.

Sergent, O., Morel, I., Chevanne, M., Cillard, P. and Cillard, J. 1995. Oxidative stress induced by ethanol in rat hepatocyte cultures. *Biochemistry and Molecular Biology International* 35: 575-583.

Sewer, M.B., Koop, D.R. and Morgan, E.T. 1996. Endotoxemia in rats is associated with induction of the P-450 4A subfamily and suppression of several other forms of cytochrome P-450. *Drug Metabolism and Disposition* 24: 401-407.

Sharma, O.P., Dawra, R.K. and Makkar, H.P.S. 1988. Effect of polymorphic crystal forms of lantana toxins on icterogenic action in guinea pigs. *Toxicology Letters* 42: 29-37.

Shull, L.R., Buckmaster, G.W. and. Cheeke, P.R. 1979. Effect of dietary selenium status on in vitro hepatic mixed-function oxidase enzymes of rats. *Journal of Environmental Pathology and Toxicology* 2: 1127-1138.

Skakun, N.P. and Vysotskiĭ, I. 1983. Vitamin E and selenium-containing preparations in the prevention treatment of tetracycline-induced lesions of the liver. *Antibiotiki* 28: 608-612.

Slater, T.F. 1984. Free radical mechanisms in tissue injury. *Biochemical Journal* 222: 1-15.

Smith, B.L. and Miles, C.O. 1993. A role for *Brachiaria decumbens* in hepatogenous photosensitisation of ruminants. *Veterinary and Human Toxicology* 35: 256-257.

Smith, K.A. and Mengel, C.E. 1968. Association of iron-dextran-induced hemolysis and lipid peroxidation in mice. *Journal of Laboratory and Clinical Medicine* 72: 505-510.

Smith, P.K., Krohn, R.I., Hermanson, G.T., Mallia, A.K., Gartner, F.H., Provenzano, M.D, Fujimoto, E.K., Goeke, N.M., Olson, B.J. and Klenk, D.C. 1985. Measurement of protein using bicinchoninic acid. *Analytical Biochemistry* 150: 76-85.

Soden, J.S., Devereaux, M.W., Haas, J.E. and Gumpricht, E. 2007. Subcutaneous vitamin E ameliorates liver injury in vivo model of steatocholestasis. *Hepatology* 46: 485-495.

Sparg, S.G., Light, M.E. and Van Staden, J. 2004. Biological activities and distribution of plant saponins. *Journal of Ethnopharmacology* 94: 219-243.

Stonard, M., Howson, S., Hughes, K. and Jackson, J. 1987. Plasma bile acid levels and enzyme activities in experimental rat models of hepatotoxicity. *Journal of Veterinary Medicine* 43: 140-147.

Stur, W.W. and Shelton, H.M. 1991. Review of forage resources in plantation crops of Southeast Asia and the Pacific. In: Shelton, H.M., Stur, W.W. (Eds.), *Forages for Plantation Crops*. Proceedings of a Workshop, Sanur Beach, Bali, Indonesia, 27–29 June 1990. pp. 25–31. ACIAR Proceedings No. 32. ACIAR, Canberra, Australia.

Sturgill, M.G. and Lambert, G.H. 1997. Xenobiotic-induced hepatotoxicity: mechanisms of liver injury and methods of monitoring hepatic function. *Clinical Chemistry* 43: 1512-1526.

Suparjo, N.M. and Abdul Wahid, S. 1980. "Pamberian rumput jenis *Brachiaria decumbence* pada kambing dan biri-biri". (Feeding of *Brachiaria decumbence* to goats and sheep). Presented at *Mal. Vet. Assoc. Confer.*, 22-24 November, pp. l2, Kuala Lumpur, Malaysia.

Takenaka, Y., Miki, M., Yasuda, H. and Mino, M. 1991. The effect of α-tocopherol as an antioxidant on the oxidation of membrane protein thiols induced by free radicals generated in different sites. *Archives of Biochemistry and Biophysics* 285: 344-350.

Tietze, F. 1969. Enzymic method for quantitative determination of nanogram amounts of total and oxidized glutathione: applications to mammalian blood and other tissues. *Analytical Biochemistry* 27: 502–522.

Tiwary, A.K. 2004. *Differences between inorganic and organic selenium toxicosis in sheep.* Thesis of MSc, Utah State University.

Tokarniaa, C.H., Dobereiner, J. and Peixoto, P.V. 2002. Poisonous plants affecting livestock in Brazil. *Toxicon* 40: 1635-1660

Torres, M.B. and Coelho, K.I. 2003. Foamy macrophages in the liver of cattle fed *Brachiaria brizantha* hay. *Veterinary and Human Toxicology* 45: 163-164.

Traber, M. and Atkinson, J. 2007. Vitamin E, antioxidant and nothing more. *Free Radical Biology and Medicine* 43: 4-15.

Traber, M.G. 2006. Vitamin E. In: Shils, M.E., Shike, M., Ross, A.C., Caballero, B. and Cousins, R. (Eds). *Modern Nutrition in Health and Disease*. 10th ed. pp. 396-411. Baltimore, MD: Lippincott Williams and Wilkins.

Traber, M.G. 2007. Vitamin E regulatory mechanisms. *Annual Review of Nutrition* 27: 347-362.

Turan, B., Acan, N.L., Ulusu, N.N. and Tezcan, E.F. 2001. A comparative study on effect of dietary selenium and vitamin E on some antioxidant enzyme activities of liver and brain tissues. *Biological Trace Element Research* 81: 141-152.

Uhlig, S., Wisløff, H. and Petersen, D. 2007. Identification of the cytotoxic constituents of *Narthecium ossifragum* (L.) Huds. using bioassay-guided fractionation. *Journal of Agricultural and Food Chemistry* 55: 6018-6026.

Urano, S., Inomori, Y., Sugawara, T., Kato, Y., Kitahara, M., Hasegawa, Y., Matsuo, M. and Mukai, K. 1992. Vitamin E: inhibition of retinol-induced hemolysis and membrane-stabilizing behavior. *Journal of Biological Chemistry* 267: 18365-18370.

Usuki, F., Yasutake, A., Umehara, F., Tokunaga, H., Matsumoto, M., Eto, K., Ishiura, S. and Higuchi, I. 2001. In vivo protection of a water-soluble derivative of vitamin E, Trolox, against methylmercury-intoxication in the rat. *Neuroscience Letters* 304: 199-203.

Valle, C.B.D.O., Calixto, S. and Amezquita, M.C. 1993. *Agronomic evaluation of Brachiaria germplasm in Brazil*. In: International grassland, 17. Proceedings. Palmerston North, New Zealand, Rockampton, Australia. pp. 511-512.

Van Cauwenbergh, R.V., Robberectht, H. and Va Vlaslaer, V. 2004. Comparison of the serum selenium content of healthy adults living in the Antwerp region (Belgium) with recent literature data. *Journal of Trace Elements in Medicine and Biology* 18: 99-112.

Vatassery, G.T., Bauer, T. and Dysken, M. 1999. High doses of vitamin E in the treatment of disorders of the central nervous system in the aged. *The American Journal of Clinical Nutrition* 70: 793-801.

Vollmar, B. and Menger, M.D. 2008. The hepatic microcirculation: mechanistic contributions and therapeutic targets in liver injury and repair. *Physiological Reviews* 89: 1269-1339.

Von Herbay, A., Stahl, W. and Niederau, C. 1997. Vitamin E improves the amino-transferase status of patients suffering from viral hepatitis C: a randomized, double-blind, placebo-controlled study. *Free Radical Research* 27: 599-605.

Von Uexküll, H.R. and Mutert, E. 1995. Global extent, development and economic impact of acid soils. In: *Plant–Soil Interactions at Low pH: Principles and Management-Date*, R.A., Grundon, N.J., Raymet, G.E. and Probert, M.E., (Eds). pp. 5-19. Dordrecht, the Netherlands: Kluwer Academic Publishers.

Wangher, P.D. 2001. Selenium and the brain: A review. *Nutritional Neuroscience* 4: 81–97.

Wang, S., Kuo, J., Choub, R.R. and Lip, C. 1996. Vitamin E protection of cell morphology and protein thiols in rat hepatocytes treated with tert-butyl hydroperoxide. *Toxicology Letters* 89: 91-98.

Wang, Y.M., Madanat, F.F., Kimball, J.C., Gleiser, C.A., Ali, M.K., Kaufman, M.W. and Van Eys, J. 1980. Effect of vitamin E against adriamycin-induced toxicity in rabbits. *Cancer Research* 40: 1022-1029.

Weber, P., Bendich, A. and Machlin, L.J. 1997. Vitamin E and human health: rationale for determining recommended intake levels. *Nutrition* 13: 450-460.

Weiss, W., Colenbrander, V., Cunningham, M. and Callahan, C. 1983. Selenium/-Vitamin E: Role in disease prevention and weight gain of neonatal calves. *Journal of Dairy Science* 66: 1101-1107.

Whanger, P.D. 2002. Selenocompounds in plants and animals and their biological significance. *Journal of the American College of Nutrition* 21: 223–232.

Williams, R.J.P. 1978. Selenium. In: Williams, R.J.P. and Da Silva, J.R.R.F. (Eds.), *New Trends in Bioorganic Chemistry*, pp. 253-260. Academic Press, London.

Wina, E., Budiarsana, I.G.M., Tangendjaja, B. and Gunawan, A. 1994. The effect of PEG and lime on Ca *Niandra calothyrsus* on its nutrients digestibility in sheep performance. *Ilmu Peternakan* 8: 13-17.

Winterbourn, C.C. 2008. Reconciling the chemistry and biology of reactive oxygen species. *Nature Chemical Biology* 4: 278-286.

Wisløff, H., Flaøyen, A., Ottesen, N. and Hovig, T., 2003. *Narthecium ossifragum* (L.) Huds. causes kidney damage in goats: morphologic and functional effects. *Veterinary Pathology* 40: 317-327.

Wisløff, H., Gharehnia, B., Flaøyen, A. and Andersen, K.J. 2007. Effects of 3-methoxy-2(5H)-furanone-containing extracts from *Narthecium ossifragum* (L.) Huds. on renal tubular cells in vitro. *Toxicon* 49: 368-377.

Wisløff, H., Uhliga, S., Scheie, E., Loader, J., Wilkins, A. and Flaøyen, A. 2008. Toxicity testing of saponin-containing *Yucca schidigera* Roetzl juice in relation to hepato- and nephrotoxicity of *Narthecium ossifragum* (L.) Huds. *Toxicon* 51: 140-150.

Wisloff, H., Wilkins, A.L., Scheie, E. and Flaøyen, A. 2002. Accumulation of sapogenin conjugates and histological changes in the liver and kidneys of lambs suffering from Alveld, a hepatogenous photosensitisation disease of sheep grazing *Narthecium ossifragum. Veterinary Research Communications* 26: 381-396.

Wong, C.C. 1980. Productivity and chemical composition of 20 improved tropical grasses in the humid tropics. *MARDI Research Bulletin* 8: 163–173.

Wong, C.C., Chen, C.P. and Ajit, S.S. 1982. A report on pasture and fodder introducetion in MARDI. *MARDI Report* no. 76. pp. 35.

Wood, A.W., Ryan, D.E., Thomas, P.E. and Levin, W. 1983. Regio- and stereoselective metabolism of two C l9 steroids by five highly purified and reconstituted rat heoatic cytochrome P-450 isozvmes. *Journal of Biological Chemistry* 258: 8839-8847.

Yen, F.L., Wu, T.H., Lin, L.T. and Lin, C.C. 2007. Hepatoprotective and antioxidant effects of *Cuscuta chinensis* against acetaminophen-induced hepatotoxicity in rats. *Journal of Ethnopharmacology* 20: 123-128.

Younes, M. and Siegers, C.P. 198I. Mechanistic aspects of enhanced lipid peroxidation following glutathione depletion in vivo. *Chemico-biological Interactions* 34: 257-266.

Yu, B.P. 1994. Cellular defenses against damage from reactive oxygen species. *Physiological Reviews* 74: 97–107.

Zamri-Saad, M., Sharif, H. and Abas, M.O. 1987. Pathological changes in indigenous sheep of Malaysia following grazing on *Brachiaria decumbens. Kajian Veterinar* 19: 9-12.

Zandi, P.P., Anthony, J.C. and Khachaturian, A.S. 2004. Reduced risk of Alzhiemer disease in uses of antioxidant vitamin supplements: the cache country study. *Archives of Neurology* 61: 82-88.

Zhang, S.S., Noordin, M.M., Rahman, S.O. and Haron, M.J. 2001. The effect of zinc supplementation on antioxidant and lipid peroxidation status during *Brachiaria decumbens* intoxication in sheep. *Veterinary and Human Toxicology* 43: 83-87.

Zhang, S.S. 2000. *Studies on the aetiopathogenesis and prevention of Brachiaria decumbens intoxication in sheep in Malaysia*. Thesis of PhD, Universiti Putra Malaysia.

Zimmerman, H.J. and Maddrey, W.C. 1993. Toxic and drug-induced hepatitis. In: L. Schiff and E.R. Schiff, (Eds). *Diseases of the liver*. 7th ed. pp. 707-783. JB Lippincott. Philadelphia.