A model for exploring lactic acidosis : 1. Model description

Zhaokun Ding and Youqing Xu

Faculty of Animal Sciences and Technology, Guangxi University, 100 Daxue Road, Nanning, Guangxi, 530004, P. R. China.
711-35 Charles St. West, University of Toronto, Toronto, ON, M4Y 1R6, Canada.
Faculty of Science, University of New England, N.S.W. 2351, Australia.
Corresponding author : Youqing Xu, e-mail : youqing.xu@hotmail.com

ABSTRACT. Incorporating our experimental data with information in the literature, a computer model was developed using the program STELLA II to study acid production and absorption, to predict the concentrations of volatile fatty acids (VFAs) and lactic acid as well as pH, and to control acid-base balance during rumen fermentation in sheep. The features of this model are based on authors' experimental data and these data have been supplemented by and checked against a wide range of additional information described in the scientific literature. The rate of buffering capacity and the relative rates of absorption of VFAs and lactic acid from the rumen were used to control lactic acid build up that are novel of this model. This model is a first step in the building of a rumen model suitable for exploring lactic acidosis.

KEY WORDS : model, volatile fatty acids, lactic acid, acidosis, rumen, sheep.

INTRODUCTION

The importance of the rumen fermentation as a means of digestion is demonstrated by the high proportion (64 - 71%) of digesta residing in the rumen relative to the whole digestive tract in cattle and sheep. It has been estimated that about 88% of VFAs produced in the rumen of sheep are directly absorbed from the rumen and only about 12% flow to the omasum (SUTHERLAND, 1963; DING, 1997).

Mechanistic model is increasingly being used as a research tool. Following the work of BALDWIN et al. (1970), some models of whole rumen function have been developed (DIJKSTRA et al., 1992; POPPI et al., 2001; KEUNEN et al., 2002; KNOTT & KERNER, 2003; KOHN, 2003). These models have endeavoured to represent the digestion and passage of ingested nutrients, microbial metabolism and the formation of end products of digestion. The use of model in optimization of rumen processes has been reviewed in different ideas (BANNINK et al., 1997; LOPEZ et al., 1999; ZIEMER et al., 2000). Although a number of issues related to rumen model require further research, the model of whole rumen function has advanced greatly over the last few decades. The whole rumen function models provide a framework to integrate knowledge on various features of rumen fermentation from which to predict the supply of nutrients to ruminants. However, so far the rumen models do not focus on the development and prevention of lactic acidosis.

Lactic acidosis arising from rapid fermentation of carbohydrate is widespread in ruminant production systems and is a condition with severe consequences for the animal (NIKOLOV, 1996, 1998; PATRA et al., 1996; DING & XU, 2003). There is a complex range of factors leading to the development of lactic acidosis (ROWE, 1997; DING et al., 1998; MULLER et al., 2002; BECKER et al., 2004). The control of the concentrations of lactic acid and volatile fatty acids (VFAs) as well as pH in the rumen during rumen fermentation is becoming the focus of more and more research in this area. As our understanding improves, a computer model of fermentation in the rumen of sheep fed grain as a dietary supplement has a potential role in predicting animal responses to different feeds, processing techniques and feeding patterns.

The objective of this study was to develop a computer model of rumen fermentation integrating knowledge on the development and control of lactic acidosis in the rumen so that we can investigate effective methods and their mechanisms for the prevention and treatment of lactic acidosis. The present paper defines the model and the data used in developing the model to explore lactic acidosis in the rumen of sheep.

THE MODEL

The model was developed using the software 'STELLA II' (High Performance Systems Inc. 45 Lyme Road, Suite 300, Hanover, NH) and was run on a Macintosh computer.

Overall structure and notation

The model is presented schematically in Fig. 1. The abbreviations used to denote entities in the model are given in Table 1. A rumen size of five liters was used as being representative of an adult sheep (DIJKSTRA et al., 1992; DIJKSTRA & FRANCE, 1996; DING, 1997). Many of the features of this model are based on experimental data described by DING et al. (1996, 1997, 1998), DING (1997), and DING & XU (2003). These data have been supplemented by and checked against a wide range of additional information described in the scientific literature as indicated in the following sections.

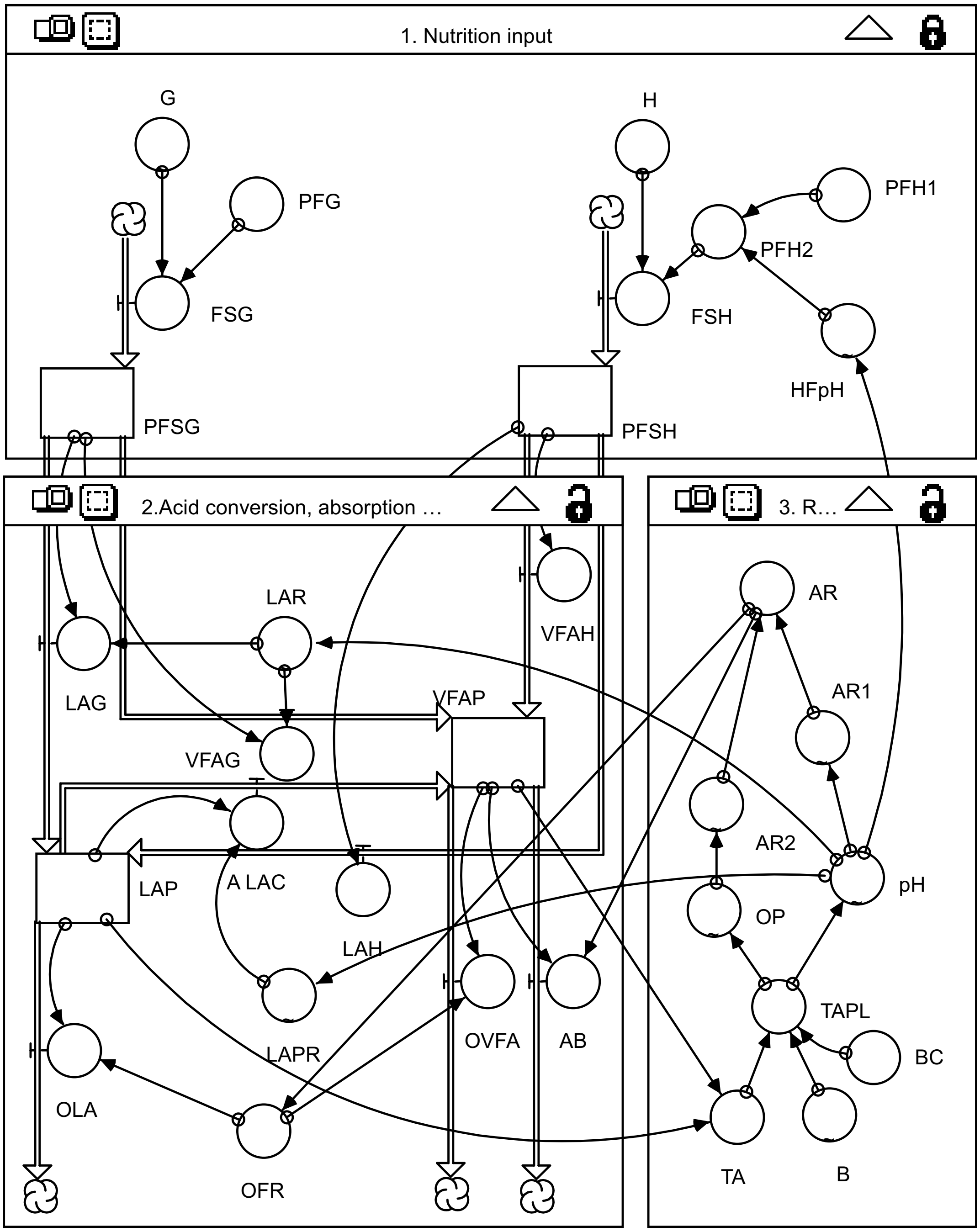

Fig. 1. – **Diagrammatic representation of the model for the rumen fermentation of sheep.** The model includes three major sections : (i) nutritional input; (ii) acid conversion, absorption and outflow; and (iii) regulation. The rectangular boxes indicate pools or state variables. The circles indicate metabolites, absorption and outflow of acids, and regulating factors. Spirals indicate beginnings or ends. Arrows indicate fluxes. Locks and triangles indicate the states and directions of three major sections, respectively.

TABLE 1

General notation used in the model

Notation	Description	Unit
G	Grain 'intake'	g/min
PFG	Potential fermentability of grain	mmol acids produced/g
FSG	Fermentable substrate produced from grain	mmol acids/min
PFSG	Pool of fermentable substrate producing acids from grain	mmol acids
H	Hay 'intake'	g/min
PFH1	Potential fermentability of hay	mmol acids produced/g
HFpH	Effect of pH on hay ferment ability	% of PFH1
PFH2	Actual fermentability of hay as determined by the effects of pH	mmol acids produced/g
FSH	Fermentable substrate produced from hay	mmol acids/min
PFSH	Pool of fermentable substrate producing acids from hay	mmol acids
LAR	Proportion of PFSG converted to lactic acid	% of PFSG
LAG	Lactic acid (LA) produced from grain	mmol/min
LAH	Lactic acid produced from hay	mmol/min
VFAG	VFAs produced from grain	mmol/min
VFAH	VFAs produced from hay	mmol/min
LAP	Lactic acid pool	mmol
VFAP	VFAs pool	mmol
LAPR	Proportion of LAP converted to VFAs	% of LAP
ALAC	Amount of lactic acid converted to VFAs	mmol/min
TA	Total amount of lactic acid and VFAs in 5-liter rumen	mmol acids
TAPL	Total acid concentration per liter (TA/5)	mmol acids/L
B	Buffer 'intake'	g/min
BC	Buffering capacity for 1 g $NaHCO_3$	mmol acids
OP	Osmotic pressure	mOsmol/kg
AR1	Absorption rate 1 (pH effect on VFAs absorption rate)	% of VFAP/min
AR2	Absorption rate 2 (Osmotic pressure effect on VFAs absorption rate)	% of VFAP/min
AR	Absorption rate of VFAs	% of VFAP/min
AB	Absorption of VFAs	mmol/min
OFR	Outflow rate of LA and VFAs in rumen fluid	% of VFAP/min
OLA	Outflow of lactic acid in rumen fluid	mmol/min
OVFA	Outflow of VFAs in rumen fluid	mmol/min

The following description of the model involves the three parts shown in Fig. 1 : 1) nutrition input; 2) acid conversion, absorption and outflow; and 3) regulation.

Nutrition input

The 'diet' in the model can be set for any ingredients and the period over which the model runs can be set for any duration. However, basically, dietary nutrients entering the 'rumen' included grain and hay, and running time was normally 24 h (1440 min). The iteration interval was set at 1 min. Therefore, all flows of material are described in g/min or mmol/min. 'Intake' levels for the basic investigation of the model were set at 300 g/d grain and 700 g/d hay. The pattern of 'intake' of grain (G) and hay (H) can be altered in the model. For basic model, the grain component of the ration of 300 g/d was 'fed' separately and 'consumed' over a 3 h period and therefore entered the 'rumen' at a constant rate of 1.667 g/min during this time. The hay ration of 700 g/d entered the 'rumen' over the full 24 h period at a constant rate of 0.486 g/min.

The grain and hay in the rumen are 'fermented' and converted to metabolites, such as acids (VFAs, lactic acid etc.). These 'precursors' or 'products' are described as follows :

FSG = G * PFG . . . . (1a)

FSH = H * PFH2 . . . . (1b)

where FSG (mmol acids/min) and FSH (mmol acids/min) are the fermentable substrates from grain and hay capable of producing organic acids. Their values are the mass of grain (G) and hay (H) multiplied by potential fermentability of grain (PFG) and actual fermentability of hay (PFH2), respectively.

The actual fermentability of hay (PFH2, mmol acids produced/g) was calculated from the potential fermentability of hay (PFH1, mmol acids produced/g) multiplied by the effect of pH on hay fermentability (HFpH, % of PFH1) (Ding et al., 1997; Ding, 1997; Rowe, 1997). The potential fermentability of hay (PFH1) was modified in this way to take account of the negative effect of acidic conditions on fiber digestion.

PFH2 = PFH1 * HFpH . . . . (2)

The potential fermentabilities of grain (PFG) and hay (PFH) were set at 8-mmol acids produced/g and 5.5-mmol acids produced/g, respectively (Leng & Leonard, 1965; Bergman et al., 1965; Weller et al., 1967; Bergman, 1990; Murray et al., 1990).

One of the most important factors influencing the fermentable substrate derived from hay in the rumen is pH. The pH effect on hay fermentability (HFpH, % of PFH1) was included as a function by which the pH altered fermentation of hay, however, the effect of pH on fermentation rate of hay would not differ significantly between different diets of hay (Tilley et al., 1963; Rowe, 1983; Rowe et al., 1991). Therefore, for the effect of pH used in the model as the parameter of HFpH, the extent of fermentation at pH 6.5 was taken to be maximal (1, i.e. 100%) and was reduced to 0.685 (68.5%) of the maximum rate with decreasing pH to 5.5 (Ding, 1997; Rowe, 1997). In the model, lactic acid and VFAs are produced from the pools of fermentable substrates from grain (PFSG) and hay (PFSH). The pools are the state variables calculated as follows (Ding, 1997; Rowe, 1997) :

PFSG(t) =

PFSG (t - dt) + (FSG - LAG - VFAG) * dt . . . (3a)

PFSH(t) =

PFSH(t - dt) + (FSH - VFAH - LAH) * dt. . . . (3b)

where t is time in min from the beginning of the simulation and dt is the time step (1 min). FSG and FSH have been defined in Equations 1a and 1b. LAG, VFAG, LAH and VFAH will be defined in Equations 4a, 4b, 5a and 5b, respectively.

Acid conversion, absorption and outflow

Acid conversion

Lactic acid and volatile fatty acids (VFAs) are produced by fermentation of both grain and hay. The percentages of lactic acid and VFAs production are determined by rate of fermentation and pH (Tilley et al., 1963; Leng & Leonard, 1965; Leng & Brett, 1966; Weston & Hogan, 1968). Lactic acid does not normally accumulate in the rumen of a sheep fed hay (Gall et al., 1953; Jayasuriya & Hungate, 1959; Nakamura et al., 1971). However, in sheep fed grain-based diets, lactic acid can accumulate with rapid fermentation and reduced rumen pH (Rowe, 1997; Rowe et al., 1991). The relationship between lactic acid production and pH is an inverse one, where increases in lactic acid production lead to a reduction in pH (Dunlop, 1972; Rowe, 1983, 1997; Rowe et al., 1991, 1993). The relationship between lactic acid production and pH used in the model can be seen in Fig. 2.

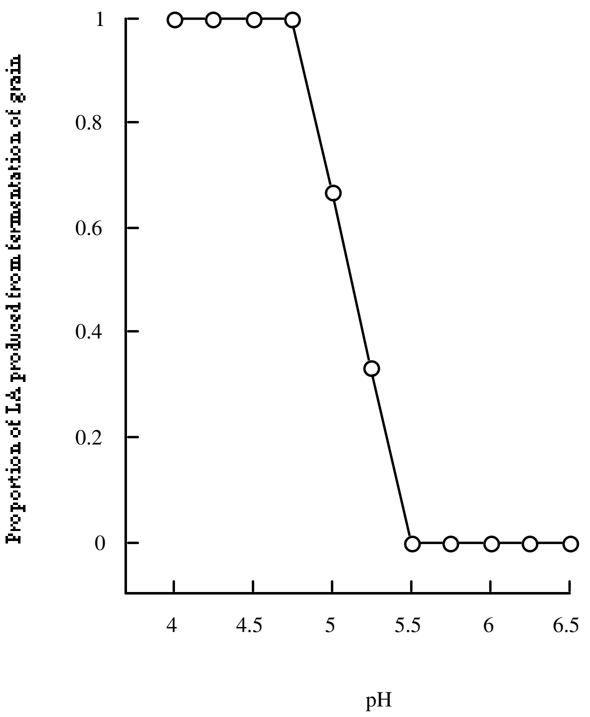

Fig. 2. – **The relationship between the proportion of lactic acid production (LAR) and pH in the rumen of sheep.** A level of 1 (100%) indicates lactic acid as the sole end-product of fermentation; while zero indicates fermentation of grain through to VFAs (adapted from Rowe et al, personal communication; Ding 1997).

Equations 4a and 4b describe the production of lactic acid from grain and hay, respectively (Tilley et al., 1963; Weston & Hogan, 1968; Rowe, 1983; Rowe et al., 1991; Godfrey et al., 1992).

LAG = PFSG * LAR . . . . (4a)

LAH = PFSH * 0.01. . . . . (4b)

where LAR is the proportion of the pool of fermentable substrate from grain (PFSG) converted to lactic acid and varies depending on pH. LAG (mmol/min) is the amount of lactic acid produced from the pool of fermentable substrate from grain (PFSG) and is mostly influenced by pH via LAR. LAG is calculated by multiplying PFSG by LAR. However, LAH (mmol/min) is the amount of lactic acid produced from the pool of fermentable substrate from hay (PFSH) and is not affected by pH. LAH produced from PFSH was negligible and constant at 0.01 (1%) (Jayasuriya & Hungate, 1959; Nakamura et al., 1971). The remaining PFSG and PFSH are converted to VFAs using Equations 5a and 5b, respectively (Weston & Hogan, 1968; Rowe, 1983; Rowe et al., 1991; Ding, 1997).

VFAG = PFSG * (1- LAR) . . . . (5a)

VFAH = PFSH * 0.99 . . . . (5b)

where VFAG (mmol/min) is the amount of VFAs produced from the pool of fermentable substrate derived from grain (PFSG) and is most influenced by pH via LAR which depends on pH. VFAH (mmol/min) is the amount of VFAs from the pool of fermentable substrate produced from hay (PFSH). A further two state variables, namely LAP (LA pool, mmol) and VFAP (VFAs pool, mmol), are used in the model and their initial values were 0 and 500 mmol, respectively (Rowe, 1983; Rowe et al., 1991; Ding, 1997). However, their values at any time (t) are expressed as :

LAP(t) = LAP(t - dt) +
(LAG + LAH - OLA - ALAC) * dt . . . . (6a)

VFAP(t) = VFAP(t - dt) +
(VFAH + VFAG + ALAC - AB - OVFA)*dt. . (6b)

where t is time in min from the beginning of the simulation and dt is the time step (1 min). LAG and LAH have been defined in Equations 4a and 4b, respectively. OLA (mmol/min) and OVFA (mmol/min) are the amount of outflow of lactic acid and VFAs from the rumen in the fluid phase, respectively (Weston & Hogan, 1968; Ding, 1997). ALAC (mmol/min) is the amount of lactic acid converted to VFAs and is calculated as follows :

ALAC = LAP * LAPR. . . . . (7)

where LAP has been defined above and LAPR (% of LAP) is the proportion of lactic acid pool converted to VFAs. Again the LAPR value depends on pH (Jayasuriya & Hungate, 1959; Patra et al., 1996; Pitt & Pell, 1997; Nikolov, 1998) and is calculated according to the relationship shown in Fig. 3.

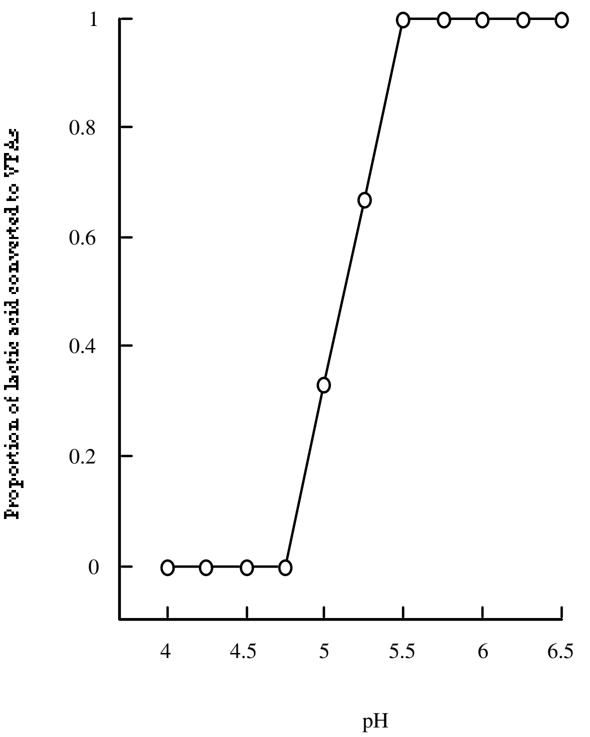

Fig. 3. – **The relationship between the proportion of the lactic acid pool converted to VFAs (LAPR) and pH in the rumen of sheep.** A level of 1 (100%) indicates conversion of all lactic acid to VFAs, while zero indicates no conversion of lactic acid to VFAs (adapted from Rowe et al., personal communication; Ding 1997; DING et al., 1997).

Acid absorption

VFAs are mainly absorbed from the rumen; however, lactic acid is apparently not absorbed from the rumen (DING et al., 1998; DING & XU, 2003). Lactic acid is either converted to VFAs or flows out of the rumen. Absorption (AB) (mmol/min) of VFAs is calculated using Equation 8 where VFAP (mmol) is the VFAs pool. AR (% of VFAP) is the absorption rate and is mainly influenced by pH and osmotic pressure (OP) (WESTON & HOGAN, 1968; GODFREY et al., 1992; ROWE, 1997; DING, 1997; DING & XU, 2003). The calculation of AR, pH and OP are described more fully in Equation 13 of the regulation section.

AB = VFAP * AR . . . . (8)

Acid outflow

In addition to fermentation and absorption in the rumen, some nutrients flow to the omasum, abomasum and the small intestine. The outflow of VFAs and lactic acid from the rumen depends on the VFAs pool (VFAP), the lactic acid pool (LAP) and outflow rate (OFR). According to the work of WESTON & HOGAN (1968), about 24% of VFAs produced in the rumen flowed out of the rumen in the fluid phase. Therefore, a value of 0.4%/min for VFAs and lactic acid was taken as the outflow rate (OFR) in Equation 9 used in the model. Again this value was dependent on the pH and osmotic pressure (WESTON & HOGAN, 1968; GODFREY et al., 1992; ROWE, 1997; DING, 1997; DING & XU, 2003).

OFR = (1 - AR)/155.6 . . . . (9)

where OFR (% of VFAP and LAP/min) is outflow rate of VFAP and LAP from the rumen. OFR is mainly affected by pH and osmotic pressure (OP) via absorption rate (AR) which varies depending on pH and OP. The constant 155.6 is calculated on the basis of AR described in Equation 13.

OVFA = VFAP * OFR . . . . (10)

where OVFA (mmol/min) is outflow of VFAs from the rumen and its value equals the product of the VFAs pool (VFAP) and the outflow rate (OFR).

OLA = LAP * OFR . . . . (11)

where OLA (mmol/min) is the outflow lactic acid from the rumen determined as the product of lactic acid pool (LAP) and outflow rate (OFR). OLA and OVFA change with pH since the formation of lactic acid (LA) and VFAs from the pool of fermentable substrate from grain (PFSG) is affected by pH (Equations 4a and 5a)

Regulation

The regulating system in the model includes buffer, pH and osmotic pressure (OP). There are many other factors, like substrate, recycling of microbial matter within the rumen, effects on digesting bacteria, affecting the regulating system (RUSSELL, 1984; JOUANY et al., 1988; ZIEMER et al., 2002; GALBRAITH et al., 2004), however, so far these informations are not fine enough to be included.

Buffer system is often included in the prevention of lactic acidosis (COUNOTTE et al., 1979; ROGERS & DAVIS, 1982; KOVACIK et al., 1986; CUMBY et al., 2001). The inclusion of additional buffer (B) is a decision variable in the model which can be altered over time Sodium bicarbonate ($NaHCO_3$) was used as a standard buffer in a series of experiments and was therefore chosen for use in this model. The buffering capacity (BC) used in the model was 15 mmol VFAs per gram of $NaHCO_3$. This is 76% of the theoretical value determined by titration in the experiments (DING, 1997; DING et al., 1996, 1997) (24% of additional $NaHCO_3$ was assumed to flow out of the rumen with the fluid or solid phase). In the experiments of DING (1997) and DING et al. (1996, 1997), it was shown that 1 g $NaHCO_3$ can buffer 20 mmol acetic acid at pH 6.

The total amount of lactic acid and VFAs present in the rumen directly affects pH. The total acids (TA, mmol) in 5 liters of 'the rumen' were considered together with the amount of additional buffer (B) to calculate the total effective acid concentration (TAPL, mmol/L) as described in Equation 12.

TAPL = (TA - B * BC)/5 . . . . (12)

where TA (mmol) is total acids, i.e. the sum of lactic acid pool (LAP) and VFAs pool (VFAP). If no additional buffer (B) is added, B * BC will be zero and TAPL will equal TA/5.

The relationships between TAPL (mmol/L), pH and OP are shown in Figs 4 and 5, respectively.

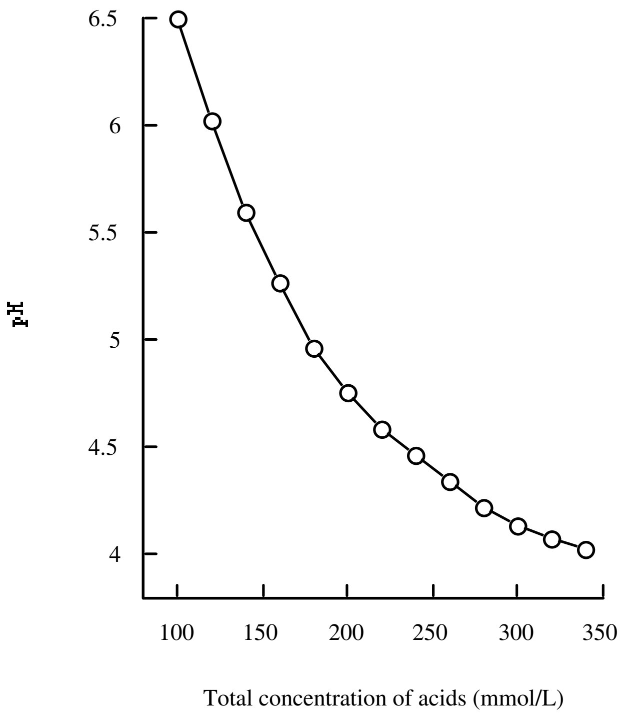

Fig. 4. – **The relationship between pH and total concentration of acids (mmol/L) in rumen digesta** (from DING 1997; DING et al., 1997).

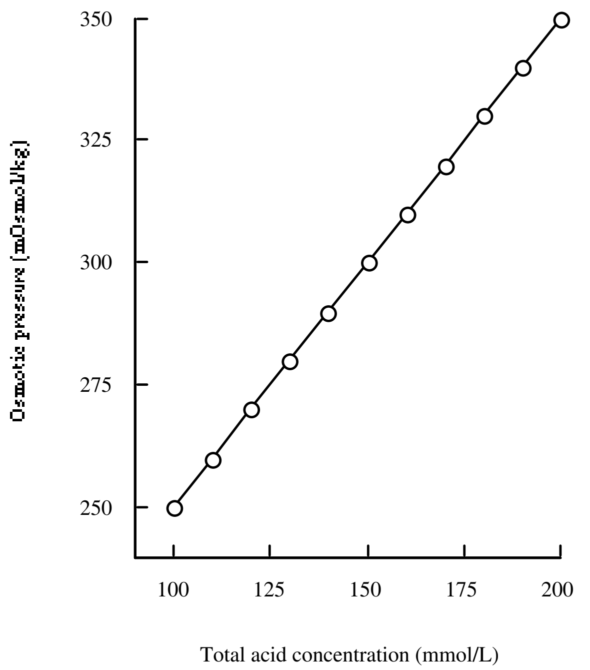

Fig. 5. – **The relationship between osmotic pressure (OP) and total concentration of acids (mmol/L) in rumen digesta** (from DING, 1997; DING et al., 1997, 1998).

The pH and osmotic pressure (OP) were found to be very important factors affecting the absorption of VFAs both in the experiments of DING et al. (1997) and the work of WILLIAMS & MACKENZIE (1965). The effects of pH and osmotic pressure (OP) on the absorption of VFAs from the VFAP in the rumen are included in the model through absorption rate 1 (AR1) and absorption rate 2 (AR2), respectively. The absorption of VFAs depends on VFAP (VFAs pool) and VFAs absorption rate (AR). AR (% of VFAP/min) was calculated in the model using Equation 13.

$$AR = AR1 * AR2/31.25 \quad (13)$$

where AR1 (% of VFAP/min) is absorption rate 1 (pH effect on VFAs absorption rate), and AR2 (% of VFAP/min) is absorption rate 2 (Osmotic pressure effect on VFAs absorption rate). The constant 31.25 is calculated on the basis of outflow rate (OFR) described in Equation 9. Equation 13 represents base rate of absorption of approximately 76%/h of VFAs production in the rumen of sheep, but it is mainly dependent on the pH, osmotic pressure and substrates (WESTON & HOGAN, 1968; DING, 1997; DING et al., 1997).

SUMMARY OF THE MODEL

All aspects of the model are represented in Equations (1) to (13) and Figs 1 to 5. Table 1 lists the abbreviations used in the Fig. 1. The differential equations can be solved numerically for a given set of initial conditions and parameter values.

This model is a first step in the building of a rumen model suitable for exploring lactic acidosis. There is another continuous paper of this model, entitling ‘a model for exploring lactic acidosis : 2. model valuation and validation’ in the same issue of this journal, to valuate the present model to key parameters and validate it by performance against experimental results in sheep.

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