(19) Europäisches Patentamt
European Patent Office
Office européen des brevets

(11) EP 1 128 738 B9

(12) **CORRECTED EUROPEAN PATENT SPECIFICATION**
Note: Bibliography reflects the latest situation

(15) Correction information:
Corrected version no 1 (W1 B1)
Corrections, see page(s) 6-9

(48) Corrigendum issued on:
24.11.2004 Bulletin 2004/48

(45) Date of publication and mention of the grant of the patent:
12.05.2004 Bulletin 2004/20

(21) Application number: **99972074.1**

(22) Date of filing: **10.11.1999**

(51) Int Cl.[7]: **A23K 1/16**, A23K 1/18

(86) International application number:
PCT/EP1999/009021

(87) International publication number:
WO 2000/028835 (25.05.2000 Gazette 2000/21)

(54) A METHOD FOR SUPPLYING BIOAVAILABLE METHIONINE TO A COW

VERFAHREN ZUR ABGABE VON BIOVERFÜGBAREM METHIONIN AN EINE KUH

METHODE D'ADMINISTRATION DE METHIONINE BIODISPONIBLE A UNE VACHE

(84) Designated Contracting States:
AT BE CH CY DE DK ES FI FR GB GR IE IT LI LU MC NL PT SE

(30) Priority: **13.11.1998 FR 9814249**
29.07.1999 FR 9910050

(43) Date of publication of application:
05.09.2001 Bulletin 2001/36

(60) Divisional application:
04010767.4 / 1 442 664

(73) Proprietor: **Adisseo Ireland Limited**
Dublin 1 (IE)

(72) Inventors:
- **ROBERT, Jean-Claude**
  F-03310 Neris les Bains (FR)
- **BENNETT, Robert**
  F-91190 Gif sur Yvette (FR)
- **GROS, Georges**
  F-92160 Antony (FR)

(74) Representative: **Guerre, Dominique et al**
Cabinet Germain et Maureau,
BP 6153
69466 Lyon Cedex 06 (FR)

(56) References cited:
WO-A-99/04647
AU-B- 478 542
FR-A- 2 305 938
US-A- 5 084 482

- **J A AYOADE ET AL: "Studies on methionine derivatives as possible sources of protected methionine in ruminant rations" JOURNAL OF THE SCIENCE OF FOOD AND AGRICULTURE,GB,ELSEVIER APPLIED SCIENCE PUBLISHERS. BARKING, vol. 33, no. 10, 1982, pages 949-956-956, XP002111468 ISSN: 0022-5142**
- **N. FOTOUHI ET AL.: "Resistance of fatty acyl amides to degradation and hydrogenation by ruminal microorganisms" JOURNAL OF DAIRY SCIENCE., vol. 75, no. 6, 1992, pages 1527-1532, XP002132143 AMERICAN DAIR SCIENCE ASSOCIATION. CHAPAIGN, ILLINOIS., US ISSN: 0022-0302**

EP 1 128 738 B9

Description

[0001] The present invention relates to a method for supplying bioavailable methionine to a cow which comprises administering to the cow an ester of the hydroxy analogue of methionine. The present invention also relates to a method of improving milk obtained from dairy cows and in particular to a method which comprises supplying to the diary cow an ester of the hydroxy analogue of methionine.

[0002] Protein is one of the major nutrients in the diets of lactating cows. The cows however do not actually require proteins but instead they require the specific amino acids, which are the building blocks that make up their own protein.

[0003] It is known that methionine is a limiting amino acid and in particular for milk production it is believed that a well balanced level of methiouine will result in effective levels of milk production. It is also believed that an increase in methionine levels can result in increased milk production.

[0004] It is therefore desirable to maintain or even enhance the level of methionine. Methionine can be added directly to the cow's diet. However, the free form of this amino acid is rapidly degraded by bacteria in the rumen and consequently only a small portion of the methionine enters the bloodstream. There have been many attempts to overcome this problem and in general the methionine is introduced into the diet in a protected or modified form, permitting the compound to pass through the rumen unaffected. The methionine released from the protected or modified form then enters the small intestine and is absorbed into the bloodstream. One of the most widely studied compounds for this particular purpose is the hydroxy analogue of methionine, namely 2-hydroxy-4-(methylthio) butanoic acid, generally refered to as HMB.

[0005] FR-A-2 305 938 or J. A. Ayoade et al., in "Studies on methionine derivatives as possible sources of protected methionine in ruminant rations", Journal of the Science of Food and Agriculture, GB, Elsevier Applied Science Publishers Barking, 33 (10), 1982, pages 949-956 ISSN: 0022-5142 discloses a ration comprising an ethyl ester of N-acetyl-L-methionine.

[0006] US-A-4,388,327 discloses a method of increasing milk production of dairy cows with the hydroxy analog of methionine and its esters.

[0007] WO 99/04647, published on 4th February 1999, discloses a method of introducing methionine into the rumen by supplementing the feed with the hydroxy analogue of methionine. In this patent application, it is claimed that the hydroxy analogue is substantially unaffected by rumen degradation, passing through the rumen and consequently providing at least 20%, preferably at least 40% of the hydroxy analogue for absorption into the bloodstream through the intestine. The patent application refers to the hydroxy analogue, its salts, esters, amides and oligomers as being 'rumen by-pass' and claims an improved efficient means of introducing methionine into the bloodstream of the cow. The claimed advantage of the disclosed compounds in this documents is that the compounds by-pass the rumen and are absorbed in the intestine.

[0008] There are also many publications on the effect of the hydroxy analogue of methionine and a publication by Charles Schwab, from a presentation given at a conference in May 1998, reviews all of the publications and concludes that the hydroxy analogue of methionine is thought to by-pass the rumen for intestinal absorption but will only do so if it is administered at a dose above 60g per animal per day, preferably above 90g per animal per day. At lower doses, it would appear, according to the author, that the hydroxy analogue of methionine is to a large extent, consumed by the micro organism in the rumen.

[0009] The best determination of the absorption of the hydroxy analogue of methionine is the determination of the bioavailability in the blood. The bioavailability is characterised by the level of appearance of methionine in the blood compared with the amount of methionine equivalent of compound introduced into the feed ration. This determination takes into account the passage of the hydroxy analogue through the rumen, its degree of absorption irrespective of the place of absorption during the digestive transit and the degree enzymatic conversion of the hydroxy analogue into methionine. At a dose of methionine equivalent to 50g per day per cow, it is described in this article that methionine protected against degradation in the rumen with a polymer, in particular the product sold under the trade name Smartamine™, has a rumen by-pass of 90%; the hydroxy analogue gives a bioavailability of only 3%.

[0010] A paper in J Dairy Science 1988, 71, pp3292 to 3301 discloses the introduction of the methyl ester or the ethyl ester of the hydroxy analogue of methionine to the diet of a cow in an attempt to increase the level of milk production. The results from the study indicate that these esters are rapidly converted to the hydroxy analogue of methionine and subsequently degraded in the rumen of the animal. Specifically, after incubation for six hours in rumen juices, only 1.8% and 3% of the methyl and ethyl ester of the hydroxy analogue respectively, remains. This is compared with 34% and 85% of methionine and the hydroxy analogue of methionine.

[0011] We have now found, contrary to the teachings of the aforementioned prior art, that a certain ester of the hydroxy analogue of methionine has a favourable effect in cows. We have surprisingly found that the compound introduces methionine into the bloodstream of the rumen more effectively and more rapidly than the known prior art. We have also found that this particular compound does not enter the bloodstream through rumen by-pass and intestinal absorption but by absorption through the rumen wall. We have also found that introducing the specific ester compound

into the diet of dairy cows through the feed ration results in desired improvement in milk production.

[0012] Accordingly the present invention provides a method for supplying bioavailable methionine to a cow which comprises administering to the cow an ester which ester is the isopropyl ester of the hydroxy analogue of methionine.

[0013] For the purposes of the present invention, by cow is meant cattle, namely beef cows and dairy cows.

[0014] The use of the claimed ester provides the advantage over the prior art in that it provides a greater amount of methionine into the bloodstream of the cow than the methionine derivatives of the prior art. Furthermore, we have surprisingly found that the use of the particular ester results in very rapid absorption of methionine into the bloodstream. The ester derivative according to the present invention appears not only to avoid rumen degradation but surprisingly to introduce methionine into the bloodstream by absorption through the rumen wall. This is contrary to the aforementioned prior art wherein the hydroxy analogue compounds of methionine are known to either degrade in the rumen or by-pass the rumen and absorb through the intestine.

[0015] As is evident from the prior art in this area, studies to introduce methionine into the bloodstream of the ruminant have concentrated on the use of rumen by-pass compounds as the quickest and most effective means of introducing methionine into the bloodstream. We have found that the addition of the ester of the present invention to the diet of the cow can result, in some cases, in more than 50% of methionine equivalent being absorbed directly through the rumen wall. Not only does this ester have a high bioavailability level but it allows methionine or biologically equivalent compounds to enter the bloodstream very quickly after intake by the cow through rumen absorption. This result is surprising and quite unexpected because until now, it has actually been believed that only compounds such as volatile fatty acids, ammonia and dioxycarbons are absorbed through the rumen wall.

[0016] The present invention also seeks to provide an improvment in the condition of the cow and the use of the specific ester of the present invention can result in an improvment in the weight gain, an improvement in the fertility, an increase in energy as well as an improvement in the function of the liver.

[0017] The effect on the liver function as a result of the administration of the ester is an important benefit. This effect may be characterised by a reduction in metabolic problems through an improvement in the very low density lipoproteins. Also thought likely, is a reduction in blood ketosis and a limitation of hepatic steatosis.

[0018] The administration of the ester can also have a beneficial effect on reproduction. The interval between calving and reproduction may be shortened. This effect is also characterised by an increase in the percentage fertilisation during insemination.

[0019] It also appears that the use of the specific ester may result in a stimulation of rumen fermentation, thus resulting in more digestible organic matter and therefore more energy.

[0020] We have also found that when the ester of the present invention is given to dairy cows, there is an improvement in the milk obtained thereof.

[0021] According to another aspect of the present invention, there is provided a method of improving milk from a dairy cow which comprises administering to the cow an ester which ester is the isopropyl ester of the hydroxy analogue of methionine.

[0022] Where the ester of the present invention is supplied to dairy cows we have found that by supplementing the normal daily feed of the dairy cow with the isopropyl ester of the hydroxy analogue of methionine, there is a surprising improvement in the quality of the milk obtained from the dairy cow. In particular, we have found that the introduction of the specific ester into the diet of the diary cow results in an increase in the protein content of the milk.

[0023] Furthermore, in addition to the protein level, it has been found that the administration of the isopropyl ester of the hydroxy analogue of methionine can result in improvements in the volume of milk produced and the fat content of the milk.

[0024] The increase in protein content as a result of the administration of the ester can be evaluated as being generally between 0.5 and 4g of protein per litre of milk. The proteins which are generally increased are alpha, beta and kappa, especially the beta and kappa proteins which have a favourable effect on the cheese making properties of the milk produced.

[0025] The foregoing objects may be obtained in whole or in part.

[0026] It has been found that the use of the isopropyl ester of the hydroxy analogue of methionine is particularly effective, being capable of providing at least 50% of methionine equivalent to the bloodstream by absorption across the rumen wall. The isopropyl ester of the hydroxy analogue of methionine has been found to display a biovailablity of methionine of more than 50%.

[0027] Furthermore it has been found that with the isopropyl ester of the hydroxy analogue, the bioavailability peak appears in the blood relatively quickly following the administration indicating, that the ester is absorbed directly through the rumen wall thus indicating that the ester is not rumen by-pass.

[0028] The ester may be supplied to the cow in any suitable way. Preferably, the ester is supplied as a feed supplement and may be supplied to the cow through the normal daily feed. Cows are fed a ration which comprises a concentrate portion and a forage portion. According to another aspect of the present invention there is provided a ration comprising a forage portion, a concentrate portion and a supplement, said supplement comprising an ester which ester is the

isopropyl ester of the hydroxy analogue of methionine.

[0029] A preferred ration comprises a forage portion, a concentrate portion and the isopropyl ester of the hydroxy analogue of methionine.

[0030] The amount of ester introduced into the feed of the cow may vary from the breed of cow and from the stage of the milk producing cycle. Suitably, the supplement comprises an amount of ester calculated as methionine equivalent of up to 75g, preferably from 5 to 50g, especially from 10 to 30g per animal per day.

[0031] The amount of ester required may be calculated using any suitable means familiar to the person skilled in the art. Suitably, the amount may be determined through the use of a computer model.

[0032] The isopropyl ester of the hydroxy analogue of methionine may be present in a concentration of from 7 to 65g per animal per day, most preferably from 10 to 30g per animal per day of ester.

[0033] According to another aspect of the present invention there is provided a unit dosage form comprising an ester which ester is the isopropyl ester of the hydroxy analogue of methionine suitable for dosage for one cow for one day.

[0034] The forage portion may typically comprise corn silage, grass silage, alfalfa silage and/or hay silage. The concentrate portion may typically comprise grains such as corn, wheat, barley in addition to sources of protein such as meal, rape seed, soyabean, corn gluten and by products such as fish meal, blood meal, brewers grain and the like.

[0035] The supplement comprising the ester may be mixed with the forage portion and the grain portion at any suitable time. The ester is a liquid and may be introduced by mixing in with the forage portion and the concentrate portion prior to the formation of the food pellets. Alternatively, the ester may be added to the pellet ration by the farmer prior to feeding to the cow.

[0036] The ester when incorporated into the feed pellet either before or after formation of the pellet is stable. It has been found that the isopropyl ester of the hydroxy analogue is stable in the resulting pellet, retaining over 95% stability over a long period. Thus, the use of the ester of the present invention as a food supplement provides a stable source of methionine.

[0037] The present invention will now be described in detail with reference to the following examples.

EXAMPLE 1:- ISOPROPYL ESTER OF THE HYDROXY ANALOGUE OF METHIONINE

(a) PREPARATION OF THE ESTER:

(1) isopropyl ester of the hydroxy analogue of methionine.

[0038] 314.4g (1.88mol) of 2 hydroxy-4 methylthio-butyronitrile was placed in a stirred jacket reactor fitted with chicanes. 201.3g (1.951 mol) of 95% sulphuric acid was added slowly whilst maintaining the temperature below 50°C. After the introduction of the acid, the reaction temperature was maintained at 45°C for 15 minutes. 227.3g of isopropanol was added to the reactor contents. The temperature of the reactor was then increased at a rate of 5°C per minute until the temperature at the bottom of the reactor reached 116°C and the temperature at the top reached 75 °C. These reactor conditions were maintained for 5 hours. Some of the distillate was removed during that period and replaced with fresh isopropanol.

[0039] The reaction mixture was then neutralised with 161.2g of 32% aqueous ammonia (2.72 mol of ammonia). Two phases were obtained. 780g of water and 449.7g of dichloromethane were added. The two resulting phases were separated to yield 939.1g of organic phase and 1247.4g of aqueous phase.

[0040] The light fractions of the organic product were removed by distillation. The temperature of the evaporating bath was increased and the pressure reduced to approximately a few milibars. 263.5g of distillate was recovered. The titre of isopropyl ester was found to be greater than 99%. The yield was 72%.

(b) BIOAVAILABILITY

[0041] Spot doses of the following amount of the ester prepared as detailed above, equating to 50g of methionine equivalent, were given to 2 cows in the manner described in Example 2(b1) above.

isopropyl ester of HMB: 80.5g

[0042] The concentration of methionine and HMB was measured over a period of 27 hours. The measurements were plotted and the areas under the curve calculated to provide the bioavailability results.

[0043] Bioavailability was determined with reference to Smartamine™.

[0044] The bioavailability results of the ester are given in Table 1

TABLE 1

BIOAVAILABILITY RESULTS

ISOPROPYL ESTER OF THE HYDROXY ANALOGUE OF METHIONINE (HMB)

Ester	Time after administration (hours)	0	1	2	3	5	7	27	Bioavailability
Isopropyl ester of HMB	[met]*	0.27	1.53	1.96	2.49	2.93	2.93	1.00	59%
	[HMB]*	0	1.90	1.00	0.99	0.38	0.30	0	

* concentration measured in mg/100g of blood plasma; met=methionine

EXAMPLE 2 : KINETICS

[0045] The kinetics of availability of methionine and HMB in the bloodstream were determined for the isopropyl ester of the hydroxy analogue of methionine and compared with the hydroxy analogue of methionine (a compound not according to the present invention).

[0046] Samples of the isopropyl ester of the hydroxy analogue (69g) and the hydroxy analogue (Alimet™ -57g) were given to four cows. The methionine and HMB levels in the blood plasma taken from the cows were analysed and the results are given in Tables 3 and 4 below.

[0047] It can be seen from the results that the isopropyl ester of the hydroxy analogue of mechioniae provides methonine and HMB to the bloodstream much quicker than HMB itself, thus indicaring the ester is absorbed through the rumen wall.

TABLE 2

BLOOD PLASMA METHIONINE CONCENTRATIONS (mg/100g of plasma)

COMPOUND	Time after administration	0	10 mins	20 mins	30 mins	40 mins	50 mins	60 mins	75 mins	90 mins	120 mins	240 mins
HMB	COW 1	0.32	0.31	0.34	0.29	0.27	0.27	0.28	0.29	0.30	0.26	0.48
HMB	COW 2	0.39	0.32	0.35	0.35	0.34	0.34	0.35	0.29	0.31	0.39	0.67
HMB	COW 3	0.40	0.35	0.36	0.36	0.34	0.34	0.34	0.31	0.33	0.42	0.59
HMB	COW 4	0.30	0.33	0.34	0.36	0.31	0.26	0.24	0.25	0.28	0.32	0.46
Isopropyl ester of HMB	COW 1	0.33	0.72	1.00	1.13	1.30	1.46	1.60	1.69	1.74	1.96	2.12
Isopropyl ester of HMB	COW 2	0.33	0.45	0.67	0.71	0.75	0.77	0.86	1.11	1.43	1.75	1.98
Isopropyl ester of HMB	COW 3	0.37	0.37	0.50	0.76	0.89	1.05	1.10	1.21	1.44	1.68	2.39
Isopropyl ester of HMB	COW 4	0.37	0.26	0.45	0.70	0.82	0.92	1.19	1.40	1.54	1.79	2.00

TABLE 3

BLOOD PLASMA HMB CONCENTRATIONS (mg/100g of plasma)

COMPOUND	Time after administration	0	10 mins	20 mins	30 mins	40 mins	50 mins	60 mins	75 mins	90 mins	120 mins	240 mins
HMB	COW 1	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.03	0.06
HMB	COW 2	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.10	0.45
HMB	COW 3	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.51
HMB	COW 4	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.24
Isopropyl ester of HMB	COW 1	0.00	4.02	4.19	3.64	3.40	3.11	2.71	2.35	2.23	1.78	0.58
Isopropyl ester of HMB	COW 2	0.00	1.05	1.24	1.31	1.39	1.46	1.53	3.11	2.38	2.54	0.82
Isopropyl ester of HMB	COW 3	0.00	0.28	0.93	1.45	1.96	1.99	2.37	2.94	3.49	3.11	1.09
Isopropyl ester of HMB	COW 4	0.00	0.17	0.57	1.22	1.36	1.84	3.31	3.73	2.37	2.31	0.92

EXAMPLE 3. : MILK PRODUCTION

Example (a) Isopropyl ester of the hydroxy analogue of methionine and the isopropyl ester of methionine

[0048] The isopropyl ester of the hydroxy analogue of methionine was given to 16 cows over a period of 8 weeks. Each cow was given daily corn silage and a supplement to cover 100% of requirement and a 115% PDIE (protein digestible in the intestine) requirement. The daily supplement consisted of 4.3 kg of a high energy concentrate which consists of 19.8% barley, 21.1% wheat, 37.5% beet pulp, 2.3% animal fat, 1.1% salts, 0.6% calcium carbonate and 1.1% sodium bicarbonate; 2.2 kg of tanned soya cake, 1kg of normal soya cake, 240g of urea and 300g of vitamin and mineral supplements.
The method according to the present invention was carried out by splitting the cows into three groups and giving the following supplement to the normal diet to provide 12.5g of bioavailable methionine per animal per day.

- Treatment 1 : 1kg of soya cake
- Treatment 2 : 1kg of soya cake 20g of polymer coated methionine (comparative example)
- Treatment 3 : 1 kg of soya cake supplemented with 3 % isopropyl ester of HMBI containing 57% equivalent methionine

[0049] The supplements were given to the cows according to the following schedule:

PERIOD				
Group*	D1 to D15	D15 to D30	D31 to D45	D46 to D60
1	Control without additive	isopropyl ester of HMB		Polymer-protected methionine
2		Control without additive	Polymer-protected methionine	isopropyl ester of HMB
3	isopropyl ester of HMB	Polymer-protected methionine	Control without additive	
4	Polymer-protected methionine		isopropyl ester of HMB	Control without additive

*4 cows per group

[0050] The results from the analyses of the milk produced are given below in Table 4

TABLE 4

RESULTS ON MILK PRODUCTION			
COMPOUND	Daily amount of milk (kg/ cow)	Butter Content of Milk g/kg	Protein Content of Milk
Control	31.4	39.1	30.1
isopropyl ester of HMB	32.3	44.3	30.8
COMPARATIVE: Polymer-protected methionine	31.4	40.3	30.9

[0051] It can be seen from the results that the addition of the isopropyl ester of the hydroxy analogue of methionine to the diet of the cow results in milk with higher fat content and higher protein content.

EXAMPLE 4 LIVER AND FERTILITY

[0052] The procedure of Example 3 was repeated and observations on the liver function and fertility of the cows were made. Substantial improvements were observed in the cows receiving the ester.

Claims

1. A method for supplying bioavailable methionine to a cow which comprises administering to the cow an ester which ester is the isopropyl ester of the hydroxy analogue of methionine.

2. A method as claimed in claim 1 in which the ester is introduced as a supplement to the feed.

3. A method of supplying at least 50% bioavailable methionine to a cow which comprises administering to the cow the isopropyl ester of the hydroxy analogue of methionine.

4. A method of improving milk obtained from a dairy cow which comprises supplying to the cow an ester which ester is the isopropyl ester of the hydroxy analogue of methionine.

5. A method as claimed in claim 4 the improvement in which comprises increased protein content in the milk.

6. A method as claimed in claim 4 the improvement in which comprises increased fat content in the milk.

7. A ration comprising a grain portion, a concentrate portion and a supplement, said supplement comprising an ester which ester is the isopropyl ester of the hydroxy analogue of methionine.

8. A ration as claimed in claim 7 in which the supplement comprises an amount of ester calculated as methionine equivalent of up to 75g.

9. A ration as claimed in claim 8 comprising an amount of ester calculated as methionine equivalent of 10 to 30g.

10. A ration as claimed in claim 7 wherein the isopropyl ester is present in an amount of from 7 to 65g per cow per day.

11. A unit dosage form comprising an amount of an ester which ester is the isopropyl ester of the hydroxy analogue of methionine suitable for dosage for one cow for one day.

12. A method of improving the condition of a cow which comprises supplying to the cow an ester which ester is the isopropyl ester of the hydroxy analogue of methionine, wherein the methods for treatment of the human or aminal body by surgery or therapy and diagnostic methods practised on the human or animal body are excluded.

13. A method as claimed in claim 12 in which the improvement comprises improved fertility.

14. A method as claimed in claim 12 in which the improvement comprises an increase in energy.

15. Use of the isopropyl ester of the hydroxy analogue of methionine for the preparation of a feed supplement for improving liver function to a cow.

Patentansprüche

1. Verfahren zur Abgabe von bioverfügbarem Methionin an eine Kuh, das **dadurch gekennzeichnet ist, daß** man an die Kuh einen Ester verabreicht, bei dem es sich um den Isopropylester des Hydroxy-Analogs von Methionin handelt.

2. Verfahren nach Anspruch 1, bei dem der Ester in Form eines Futterzusatzes bereitgestellt wird.

3. Verfahren zur Abgabe von mindestens 50% bioverfügbarem Methionin an eine Kuh, das **dadurch gekennzeichnet ist, daß** man an die Kuh einen Ester verabreicht, bei dem es sich um den Isopropylester des Hydroxy-Analogs von Methionin handelt.

4. Verfahren zur Verbesserung der von einer Milchkuh produzierten Milch, **dadurch gekennzeichnet, daß** man an die Kuh einen Ester abgibt, bei dem es sich um den Isopropylester des Hydroxy-Analogs von Methionin handelt.

5. Verfahren nach Anspruch 4, bei dem die Verbesserung einen erhöhten Proteingehalt in der Milch umfaßt.

6. Verfahren nach Anspruch 4, bei dem die Verbesserung einen erhöhten Fettgehalt in der Milch umfaßt.

7. Ration, die einen Kornanteil, einen Konzentratanteil und einen Zusatz umfaßt, wobei der Zusatz einen Ester, bei dem es sich um den Isopropylester des Hydroxy-Analogs von Methionin handelt, umfaßt.

8. Ration nach Anspruch 7, bei der der Zusatz eine als Methioninäquivalent berechnete Estermenge von bis zu 75 g umfaßt.

9. Ration nach Anspruch 8, die eine als Methioninäquivalent berechnete Estermenge von 10 bis 30 g umfaßt.

10. Ration nach Anspruch 7, in der der Isopropylester in einer Menge von 7 bis 65 g pro Kuh und Tag vorliegt.

11. Einzeldosisform, die eine für eine Dosierung für eine Kuh und einen Tag geeignete Menge eines Esters, bei dem es sich um den Isopropylester des Hydroxy-Analogs von Methionin handelt, umfaßt.

12. Verfahren zur Verbesserung des Zustands einer Kuh, das **dadurch gekennzeichnet ist, daß** man an die Kuh einen Ester, bei dem es sich um den Isopropylester des Hydroxy-Analogs von Methionin handelt, abgibt, wobei die Verfahren zur Behandlung des menschlichen oder tierischen Körpers auf chirurgischem oder therapeutischem Weg sowie Diagnostikverfahren, die am menschlichen oder tierischen Körper durchgeführt werden, ausgeschlossen sind.

13. Verfahren nach Anspruch 12, bei dem die Verbesserung eine verbesserte Fertilität umfaßt.

14. Verfahren nach Anspruch 12, bei dem die Verbesserung erhöhte Energie umfaßt.

15. Verwendung des Isopropylesters des Hydroxy-Analogs von Methionin zur Herstellung eines Futterzusatzes zur Verbesserung der Leberfunktion einer Kuh.

Revendications

1. Procédé d'administration de méthionine biodisponible à une vache, comprenant l'administration à la vache d'un ester, ledit ester étant l'ester isopropylique de l'hydroxy-analogue de la méthionine.

2. Procédé selon la revendication 1, dans laquelle l'ester est introduit en complément dans la nourriture.

3. Procédé d'administration d'au moins 50 % de méthionine biodisponible à une vache, comprenant l'administration à la vache de l'ester isopropylique de l'hydroxy-analogue de la méthionine.

4. Procédé d'amélioration du lait obtenu d'une vache laitière, comprenant l'administration à la vache d'un ester, ledit ester étant l'ester isopropylique de l'hydroxy-analogue de la méthionine.

5. Procédé selon la revendication 4, dans laquelle l'amélioration comprend l'augmentation de la teneur en protéines du lait.

6. Procédé selon la revendication 4, dans laquelle l'amélioration comprend l'augmentation de la teneur en graisses du lait.

7. Ration alimentaire comprenant une partie de céréales, une partie d'aliment concentré et un complément, ledit complément comprenant un ester, ledit ester étant l'ester isopropylique de l'hydroxy-analogue de la méthionine.

8. Ration alimentaire selon la revendication 7, dans laquelle le complément comprend une quantité d'ester calculée en tant qu'équivalent de la méthionine allant jusqu'à 75 g.

9. Ration alimentaire selon la revendication 8, comprenant une quantité d'ester calculée en tant qu'équivalent de la méthionine de 10 à 30 g.

10. Ration alimentaire selon la revendication 7, dans laquelle l'ester isopropylique est présent en une quantité comprise

entre 7 et 65 g par vache, par jour.

11. Présentation unitaire comprenant une quantité d'ester, ledit ester étant l'ester isopropylique de l'hydroxy-analogue de la méthionine, appropriée pour une ration journalière pour une vache.

12. Procédé d'amélioration de l'état d'une vache, comprenant l'administration à la vache d'un ester, ledit ester étant l'ester isopropylique de l'hydroxy-analogue de la méthionine, dans laquelle les méthodes de traitement chirurgical ou thérapeutique du corps humain ou animal et les méthodes de diagnostic appliquées au corps humain ou animal sont exclues.

13. Procédé selon la revendication 12, selon lequel l'amélioration comprend l'accroissement de la fertilité.

14. Procédé selon la revendication 12, selon lequel l'amélioration comprend l'accroissement de l'énergie.

15. Utilisation de l' ester isopropylique de l'hydroxy-analogue de la méthionine pour la préparation d'un complément alimentaire pour améliorer la fonction hépatique chez une vache.