

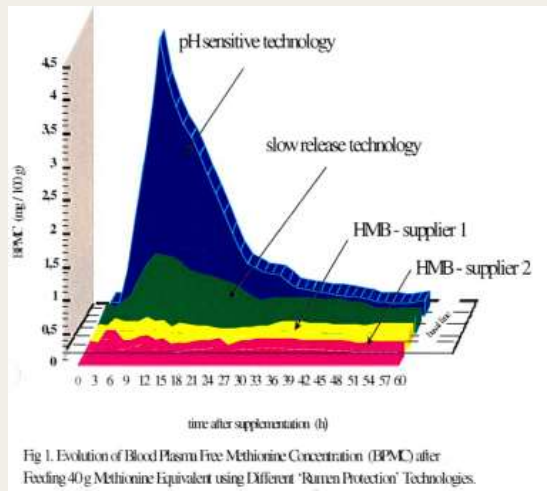
## Rumen protected methionine with pH sensitive coating

Smartamine® and Kessent™ M are rumen-protected methionine products (RPMet). A core of methionine and sodium stearate is coated by a pH-sensitive film of poly (2-vinylpyridine-co-styrene). The methionine content of the products is 75 %. The copolymer coating is highly stable under rumen pH conditions (5.5 to 6.5), but unstable at low pH around 2.5 which causes an immediate release of the methionine in the abomasum. The rumen bypass is given as > 90 % and digestibility at 90 % without any published research.

### Blood Levels and Area Under the Curve (AUC) Method

**Figure 1: Plasma methionine response curves after administration of hyper-nutritive spot doses of various RPMet sources**

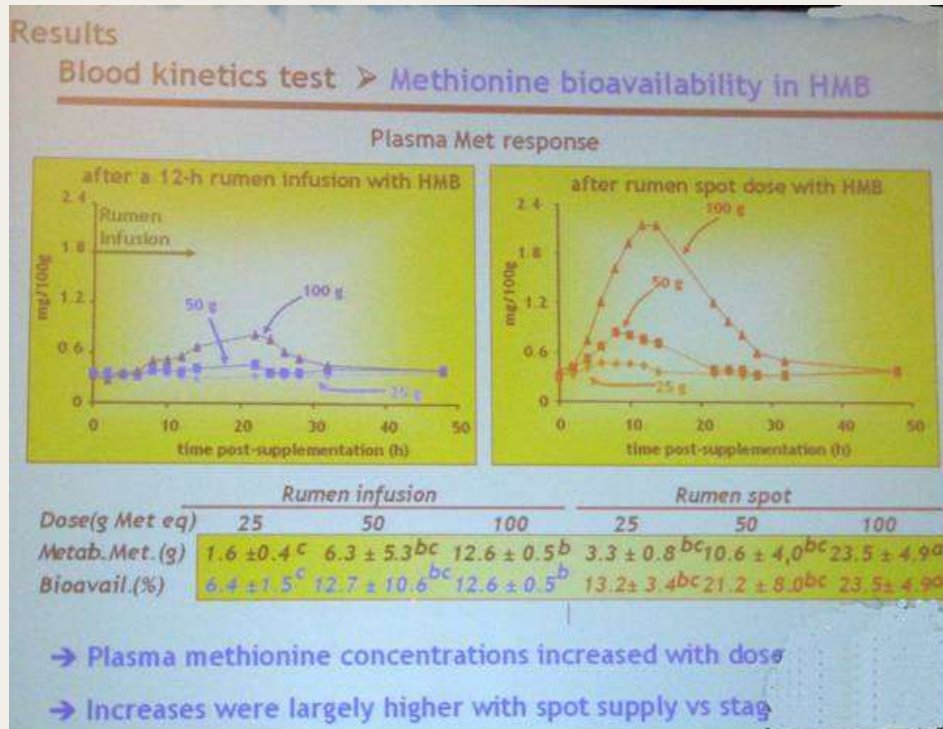
In this method, a high amount of product, typically 3 to 5 times the commercial quantity, is given in one dose, either via the feed in one meal or directly placed into the rumen of dry cows or steers. Blood plasma free methionine concentration (BPMC, Fig. 1) is analyzed at the beginning (0 h) and then at multiple times during up to 60 hours. The area under that resulting BPMC curve is used for calculating the bioavailability.



Smartamine® and Kessent™ M with its pH-sensitive coating quickly releases all its methionine after entering the acidic abomasum. Therefore, the product always shows large increases in BPMC resulting in large AUC from which Adisseo calculates the relative bioavailability for RPMet products compared to Smartamine which they set at 80 % as a standard. Using the same dose of Mepron®, the BPMC is always shown to be much lower resulting in AUC figures indicating only 20 to 40 % bioavailability. In contrast to Smartamine®'s and Kessent™ M's copolymer coating, Mepron®'s ethylcellulose coating releases methionine slowly over time by abrasion and physical forces and does not lead to high plasma methionine peaks.

Mepron® supplies methionine more continuously, and no large increase in BPMC occurs, resulting in small AUC figures. It is evident that an RPMet with slow release characteristics like Mepron® cannot be compared with a sudden release product like Smartamine® by using the AUC method. It is even stated by Adisseo that pulse dosing results in totally different (much higher) plasma levels than continuous infusion (Fig. 2, picture was taken during an Adisseo presentation at ADSA, 2005).

Figure 2: The blood kinetics test conducted and presented by Adisseo at ADSA conference (2005) clearly shows the influence of spot supply vs. continuous supply



Blood levels of amino acids are generally variable. Blood is a transport system; the levels of nutrients are controlled. Amino acids are closely regulated by the liver. Therefore, only very high doses of administered test material overwhelm the control system for some time. Because metabolic controls and interactions with other compounds affect blood levels of metabolites, results of this test are only qualitative (Wu and Papas 1997).

In such a typical artificial trial published by Südekum et al. (2004), a hyper-nutritive spot dose of 50 g of methionine equivalents was fed or even put into the rumen when not eaten in 20 minutes, resulting in a dramatic increase in BPMC of 2016 % for Smartamine®. Apart from that, bypass or digestibility numbers were not considered; only the methionine content based on specifications was used for calculating the daily product dose. Consequently, Smartamine® was fed at a higher level than Mepron®.

In a similar experiment, bypass or digestibility numbers were also not considered, only the analytical methionine content. Mepron® and Smartamine® were also fed as hyper-nutritive spot doses of 50 g methionine equivalents. Both products caused a significant rise in BPMC which was much higher for Smartamine®, but at the same time, no difference in production could be observed (Blum et al. 1999).

When Smartamine® was fed in a nutritional dose and in 3 portions per day, the BPMC increased by only 78 % (Ordway et al. 2009), which is in the same range as BPMC levels reached by Mepron® supplementation. With feeding nutritional doses of RPMet in 4 portions per day, Broderick et al. (2010) couldn't find any difference in absorption (blood levels) between Mepron® and Smartamine®.

66 studies using RPMet in dairy cows (281 diets, 2444 cows) where blood methionine was recorded were evaluated (Patton et al. 2003, TechTalk 2004). There was no correlation of blood methionine with either milk or milk protein yield.

**The Key Parameters for Evaluation of RPMet Products**

- Bioavailability of an RPMet product (%) = % Bypass x % Digestibility
- **Metabolizable Methionine (mMet)**, absorbed and available in the blood) of an RPMet product = % Met x % Bioavailability

**Smartamine®**

75 % Methionine  
90 % Bypass  
90 % Digestibility

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81 % Bioavailability  
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**60.8 % mMet**

**Mepron®**

85 % Methionine  
80 % Bypass  
90 % Digestibility

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72 % Bioavailability  
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**61.2 % mMet**

Both products deliver nearly equal amounts of mMet of about 6 g per 10 g of product fed or have a content of 60 % mMet in the commercial product.

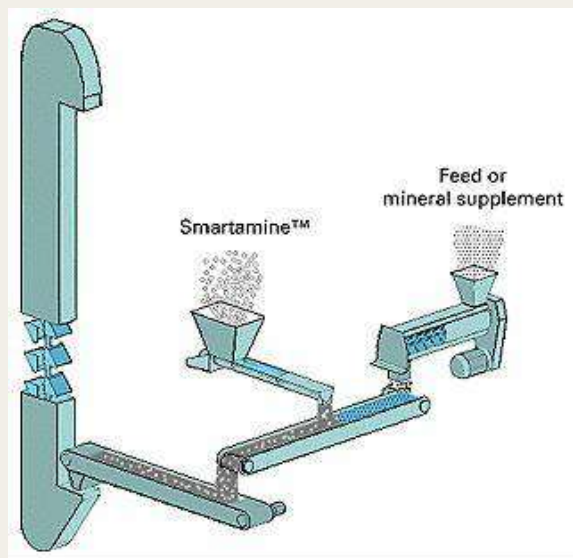
The bypass number of Mepron® was investigated by Overton et al. (1996) and Berthiaume et al. (2000) and several times in our own studies. Mepron®'s digestibility of 92 % was proven by Berthiaume et al. (2001) by quantitative measurement of mMet delivery.

**Smartamine® User's Guide**

Mepron® is stable at typical handling, mixing and conveying procedures. In contrast, a Smartamine User's Guide (Adisseo, 2015) including many pictures is required to explain which handling, mixing and conveying procedures should be avoided while using Smartamine®.

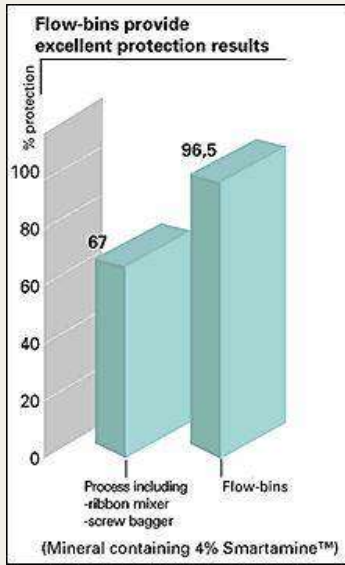
Feed production must be carried out carefully in order to maintain the coating's integrity while incorporating Smartamine® and manufacturing the feeds. Smartamine®'s coating can be damaged by physical impacts like cutting, abrasion, pressure, heat (above 40 °C) as well as prolonged exposure to wet air or humid raw materials. Smartamine® should be incorporated as close as possible to the mixer itself, for example directly above the mixer, as Smartamine® on its own can be damaged by abrasion or cutting in the machinery (Fig. 3).

Some abrasion of Smartamine® can take place during mixing. Adisseo therefore recommend keeping the dwell time of Smartamine® in mixers to a minimum and incorporating Smartamine® after homogeneity of fine components has been reached and then mixing for only 1-1.5 minutes.



**Figure 3:**  
Add Smartamine® as late as possible to avoid loss in rumen protection

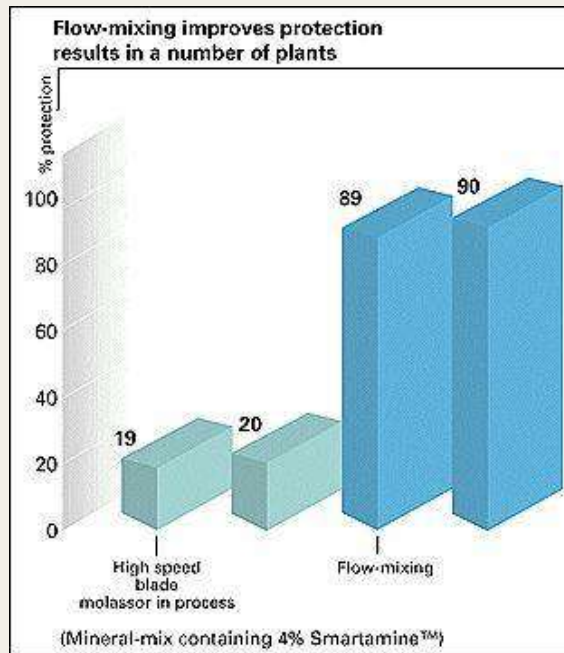
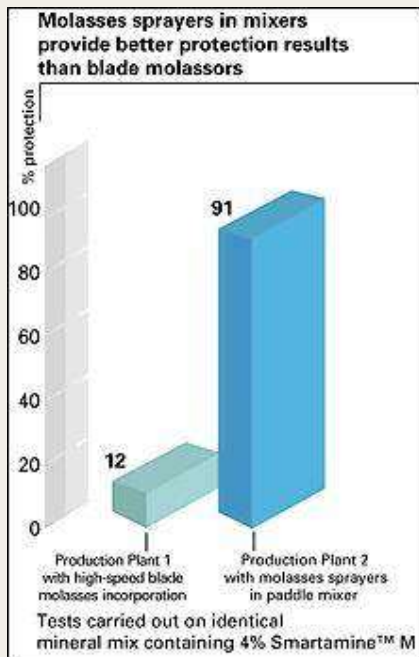
Ribbon mixers have proven to be the most potentially damaging ones to Smartamine®, ranging from 0 to 30 % loss in protection (Fig. 4). Screw baggers can inflict damage to Smartamine® (5 - 30 % loss in protection).



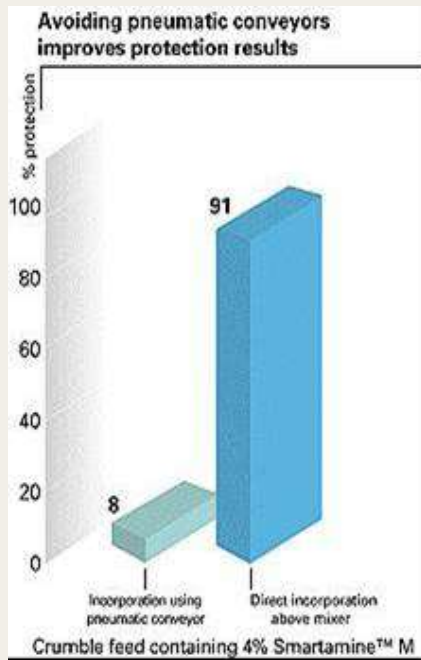
**Figure 4:** Use of ribbon mixers and screw baggers damages Smartamine®'s protection by about 30 %

Augers can damage Smartamine® due to friction created within the auger or cutting between the screw and the inner side of the auger tube. High-speed blade molasses incorporators should not be used due to severe effects on Smartamine® protection (Fig. 5 and 6).

**Figures 5 and 6:** Tremendous damage of Smartamine®'s protection through high speed blade molassors



Pneumatic conveyors should not be used, particularly for pure Smartamine® transportation (e.g. at incorporation). The use has been shown to crack Smartamine® coating, due to projection against bends in conveyor tubes. Do not use pneumatic conveyors to transfer Smartamine® to a mixer (Fig. 7).



**Figure 7:**  
Use of pneumatic conveyor destroys Smartamine®'s protection almost completely

**Because all these handling guidelines clearly show the sensitivity of the coating to handling stress, results from research with top-dressed Smartamine® cannot be transferred into practice!**

**Table 1: Summary of the Mepron® to Smartamine® technical comparison**

|                              | Mepron®  | Smartamine®   |
|------------------------------|--|---|
| Coating material             | Ethylcellulose, pH stable                                | Copolymer, labile at low pH   |
| Release technology           | Slow release and continuous methionine supply            | Fast release only in the abomasum at pH < 2.5                       |
| Features                     | 85 % Met content<br>80 % bypass<br>90 % digestibility    | 75 % Met content<br>90 % bypass<br>90 % digestibility               |
| Efficiency                   | 10 g Mepron = 6.12 g mMet                                | 10 g Smartamine = 6.08 g mMet                                       |
| Handling and mixing features | Resistant to physical stress and high temperature (85°). | Avoid all kinds of harsh treatment, must not pneumatically conveyed |

**Mepron is the more effective RPMet product**

Patton (2010) investigated the effect of RPMet on dry matter intake, milk production, true milk protein production, and milk fat yield in lactating dairy cows by using a meta-analysis including 36 full studies that had been published in refereed journals. Differences in responses between two most widely used RPMet products, Mepron® and Smartamine®, were investigated as well.

The milk protein response was twice as large for Mepron® as for Smartamine® (37 g/d vs. 16 g/d) due to the higher milk yield response for Mepron®. Milk fat yield was increased for Mepron® supplemented cows, but milk fat changes were almost non-existent for Smartamine® supplemented cows (Table 2).

**Table 2: Meta-analysis of production responses when Mepron® or Smartamine® is included in diets of lactating cows**

| Parameter                    | Adjusted mean effect by product |             |
|------------------------------|---------------------------------|-------------|
|                              | Mepron®                         | Smartamine® |
| Dry matter intake (kg)       | - 0.10                          | 0.04        |
| Milk (kg)                    | 0.35                            | - 0.22      |
| True milk protein (%)        | 0.06                            | 0.08        |
| True milk protein yield (kg) | 0.037                           | 0.016       |
| Milk fat (%)                 | - 0.01                          | - 0.02      |
| Milk fat yield (kg)          | 0.024                           | - 0.002     |

If blood values of methionine were indicators of the bioavailability of RPMet, and Smartamine® were truly more available than Mepron®, one would expect corresponding differences in the potency of these products to promote true milk protein output. This could not be observed, because Mepron® promoted milk protein synthesis more than Smartamine®. The different release properties seem to be the reason for the difference because of the more continuous methionine supply from Mepron®.

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