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TRYPSIN INHIBITOR IN SOW COLOSTRUM
AND ITS FUNCTION

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Résumé

L’INHIBITEUR DE LA TRYPSINE DANS LE COLOSTRUM DE TRUIE ET SON ROLE. — Cet article présente une courte revue bibliographique des propriétés physiques, chimiques, biochimiques, physiologiques et fonctionnelles de l’inhibiteur de la trypsine du colostrum de truie. On a centré l’intérêt sur les variations physiologiques dans le colostrum et le lait, et dans le sérum et l’urine pour les porcelets à la mamelle. La possibilité d’une relation entre l’inhibiteur et la pathologie est suggérée.

Introduction

Inhibitors of trypsin activity have been found in the colostrum of different mammalian species such as women (Laskowski and Laskowski, 1951), cows (Laskowski and Laskowski, 1951), sows (Laskowski et al., 1957), cats (Baintner, 1973), and rats (Carlsson et al., 1975). Very early it was postulated that the physiological role of the inhibitors in colostrum was to protect the colostral antibodies from digestion by trypsin (Laskowski and Laskowski, 1951). Since then, the interest has concentrated about the inhibitors from cow and sow colostrum as the newborn calves and piglets were known to be very sensitive to infection when deprived of the immunoglobulin contents in normal colostrum.

Physical and chemical properties

Sow colostrum trypsin inhibitor (SCTI) was first isolated in 1957 by Laskowski et al. The inhibitor had an ultraviolet absorption spectrum typical of proteins and was found to have a low molecular weight. Kress et al. (1971) found a heterogeneity of the inhibitor. They isolated four iso-inhibitors with only small differences in composition and with almost the same substrate specificity. Carlsson et al. (1974) determined by gel filtration the molecular weight of SCTI to be about 18,000, in contrast to the molecular weights of the serum inhibitors which were about 70,000. By electrophoresis of sow colostrum and sow serum Carlsson and Karlsson (1973) found the trypsin-inhibiting activity to be localized in the γ-region of colostrum and in the α-region of serum. Immunochemical investigations have shown that the SCTI is antigenic, and immunologically unrelated to the serum inhibitor or any other serum proteins (Jensen, 1977). Laskowski et al. (1957) found that both SCTI and the cow colostrum inhibitor were resis-
tant to acidic conditions and to pepsin with SCTI more resistant to pepsin than the inhibitor from cow colostrum. By all these criteria SCTI was found to be a specific inhibitor unrelated to the inhibitors in serum. Contrary, the inhibitors in woman and rat colostrum resemble those in human serum and rat serum (Barkholt-Pedersen et al., 1971; Weström and Carlsson, 1976). Also the cow colostrum trypsin inhibitor is a specific colostrum inhibitor (Pineiro et al., 1975).

**Biological properties**

The specific colostrum inhibitor dominates but is not the only trypsin inhibitor in sow colostrum. By preparative electrophoresis of sow colostrum Carlsson and Karlsson (1973) found a low level of trypsin inhibiting activity in fractions with a migration rate corresponding to the serum inhibitors (x-region). Gel filtration of colostrum whey on Sephadex G-100 (Jensen, 1977) showed a weak trypsin inhibiting activity in some concentrated fractions of the first elution peak (high molecular weight) and a major activity in a second small protein peak (low molecular weight). In the same investigation agreement was found between the results obtained on examination of colostrum samples by, respectively, single radial immunodiffusion using a specific antiserum against SCTI, and a radial diffusion assay with a casein substrate to measure trypsin inhibitor activity; \( r = 0.97, n = 10 \). The high correlation coefficient together with the other observations referred indicate that the specific colostrum inhibitor (SCTI) is the absolutely essential trypsin inhibitor in sow colostrum.

Laskowski et al. (1957) and Carlsson et al. (1974) found a very rapid fall in the trypsin inhibitor activity in colostrum and milk samples from a few sows during the first days of lactation; this was verified by Jensen and Pedersen (1978) who by immuno-chemical measurements on colostrum and milk samples from 9 sows found a rapid fall in the SCTI content during the first two days of lactation and a total disappearance after about two weeks. An investigation on colostrum samples collected from 58 sows during or immediately after parturition and again 24 h later showed a mean fall from about 2 g SCTI per litre to about 0.2 g SCTI per litre paralleled by a similar fall in the IgG content (Jensen, 1978). A big variation in SCTI content in whey from colostrum samples, collected in relation to farrowing, from different sows was found in the same investigation with a range from 0.8 g SCTI per litre to 4.9 g per litre. The trypsin inhibitor concentration in sow colostrum was assumed by Baintner (1973) to decrease at a rate depending on the litter size. The conclusion was based only on two litters and could hardly be verified by Jensen (1978) who found only a low insignificant negative correlation between the SCTI level one day after parturition and the litter size (\( r = -0.23, n = 58 \)).

The variation between individuals and the rapid fall in the colostrum level of SCTI during the first day of lactation make it very difficult to compare the absolute values from different investigations, a problem stressed by the different methods for determination of the inhibitor or the inhibitor activity. In the author’s experience a value of about 2 g SCTI per litre colostrum whey, corresponding to inhibition of about 5.7 g trypsin per litre, may be considered as normal in the first colostrum from Danish Landrace pigs (Jensen, 1978).

The SCTI is absorbed from the intestinal tract of the piglets in an active state and is eliminated very quickly in the urine (Baintner, 1970; Carlsson and Karlsson, 1972, 1973; Carlsson et al., 1974; Jensen, 1977). Jensen (1977) found a very low serum level during the absorption phase (0.05 g/l) but a urine level as high as the colostrum level (1.5 g/l). The urinary excretion of the low molecular trypsin inhibitor, and other low molecular proteins, giving a transient neonatal proteinuria, is assumed not to be caused by drastic changes in the function of the kidneys of the newborn piglets, but rather a consequence of temporarily high amounts of filterable low molecular proteins in urine of the colostrum fed neonatal piglets (Carlsson et al., 1974).

SCTI has been found totally to suppress trypsic activity in the intestinal lumen of newborn piglets for about three days, while the SCTI-resistant proteases made their appearance after half a day (Baintner, 1973). Kress et al. found the SCTI to be active in vitro against bovine and porcine trypsin, \( x \)-chymotrypsin and chymotrypsin B.
Biological function

The ability of newborn pigs to acquire passive systemic immunity by absorption of undigested immunoglobulins from colostrum during the first 24-36 h after onset of colostrum ingestion (Brambell, 1970) was postulated to be connected with a biological function of SCTI already before the inhibitor was isolated. In an experiment with insulin, injected into ligated jejunal loops of rats, Laskowski et al. (1958) showed that protein absorption could be increased by simultaneous application of a trypsin inhibitor, and that the effect of the inhibitor was to protect the protein (insulin) against destruction. Nordbring and Olsson (1958 a, b) found an increase in the absorption of immunoglobulins from porcine colostrum and serum after feeding purified bovine colostrum trypsin inhibitor. Barrick et al. (1954) found no effect on the appearance of γ-globulin in the blood of newborn pigs fed orally with the pepsin-sensitive soya bean inhibitor. Chamberlain et al. (1965) showed that purified SCTI was incapable of inducing the absorption of isotopically labelled γ-globulin in 3-day-old piglets. They also concluded that the disappearance of the trypsin inhibitor activity from colostrum during the first days of lactation did not account for the cessation of protein absorption. Hardy (1969) examined the absorption of isotopically labelled γ-globulin from porcine serum and found that bovine colostrum to a small degree increased the absorption of undigested γ-globulin. The effect of colostrum could be simulated by the addition of either the synthetic trypsin inhibitor Trasylol or a higher concentration of protein. In the experiments of Hardy was used bovine colostrum which normally has a much smaller trypsin inhibitor capacity than porcine colostrum (Laskowski et al., 1957). As acid pH in the stomach and proteolytic activity in the gut contents of newborn pigs have been reported (Hardy, 1969; Hartman et al., 1961) it is possible that too low levels of both immunoglobulins and trypsin inhibitor activity may be the reason for the low blood concentration of undigested immunoglobulins found in most experiments. In a preliminary experiment by the author using purified SCTI there was direct evidence for a protective effect on specific antibodies (Jensen and Pedersen, to be published). The specific inhibitory effect of SCTI on some intestinal proteases (especially trypsin) makes it possible that the colostrum inhibitor has a special ability to protect the proteins most sensitive to trypsin during the period of protein absorption as claimed by Brock et al. (1977) for the bovine colostrum trypsin inhibitor.

SCTI and pathology

Colostrum trypsin inhibitors were suggested by Griner (1963) to be of possible pathogenetical significance in enteritis in newborns caused by types of Clostridium perfringens producing β-toxin such as the C-type causing necrotizing enteritis in newborn pigs. The β-toxin is inactivated by trypsin (Dalling and Roos, 1938) and could easily be protected by the trypsin inhibitor in sow colostrum. If so, it may partly explain the high mortality among the newborn pigs (Hogh, 1967, 1974).

If the enhancement of trypsin treatment on the infectivity of some viruses in cell cultures i.e., rotavirus (Babiuk et al., 1977) also has clinical significance the SCTI may perhaps reduce the pathogenicity in newborn pigs.

Summary

A short review is given on physical, chemical, biochemical, physiological, and functional properties of sow colostrum trypsin inhibitor. Special interest is concentrated on the physiological variations in colostrum and milk, and in serum and urine from suckling piglets. Possible significance of the inhibitor in relation to pathology is suggested.

References


