Opioids in milk

Two types of opioids have been found in milk: opioids which apparently represent constituents of the milk and opioids apparently originating from other tissues, or even acquired from food ingested by the female. An opioid of this latter type was recently identified by Hazum and co-workers[1] and opioids of this type were detected in an earlier study by Brantl and Teschemacher[2].

Hazum and colleagues reported that the opiate morphine is present as a constituent of milk, apparently originating from hay or other plants taken up with food. It can be speculated that the non-peptide, morphine-like compounds found in the CNS of various species, as demonstrated by Gintzler *et al.*[3] and Killian *et al.*[4] by use of specific antibodies, may be identical with the opiate identified by Hazum *et al.*[1].

In addition to such 'foreign opioids', others, representing original milk constituents, have also been detected. Wajda *et al.*[5] described opioid activity found in casein hydrolysate but they have not reported any further studies based on this finding. Whilst extending their search for opioids to baby food and casein peptone, Brantl and Teschemacher[2] independently demonstrated the presence of opioids. These opioids have subsequently been isolated, identified and resynthesized by Brantl *et al.*[6], Henschen *et al.*[7] and Lottspeich *et al.*[8], and have been termed β-casomorphins in view of their morphine-like activity and their origin – they represent fragments of the milk protein β-casein. These, 'natural' β-casomorphins[6,9,10] and their derivatives[11–13] have been tested for pharmacological activity and have been established as mixed μ/δ-type opioid agonists. One derivative, β-casomorphin-4-amide ('morphiceptin'), which turned out to be a highly potent μ-type agonist, has been intensively studied by Chang and co-workers[12].

The physiological role of the β-casomorphins is, as yet, not clear; β-casomorphin-immunoreactive compounds seem to be generated in and absorbed from the gastrointestinal tract after ingestion of milk under certain conditions and have also been found in milk incubated with microorganisms[14,15].

Hartrodt *et al.*[16] have presented evidence that β-casomorphins, which are known to be very resistant to such proteases as pronase, trypsin, chymotrypsin and carboxypeptidases A and B[2,6,7] are degraded by dipeptidyl-peptidase IV (DPIV), thus satisfying one criterion for the characterization of a physiologically-significant compound. Havemann and Kuschinsky[17] have found that β-casomorphin-4-amide is more potent than morphine in eliciting certain CNS effects.

Further studies are required in order to obtain information about the physiological role of β-casomorphins, which may be equally as important as other compounds, for example hormones, found in milk.

Very recently, Zioudrou *et al.*[18] succeeded in splitting morphine-like fragments from α-casein; these peptides have not, as yet, been extensively investigated. It is difficult to believe that these, or other types of opioids found in the milk, can be devoid of physiological, or nutritional, significance.

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Computer Club

The world of pharmacology computing

New techniques for pharmacological data analysis

The computer in the pharmacology laboratory is increasingly finding practical application. Teaching, automated experiments and data analysis now frequently make use of a computer. In this last area, namely that of data analysis, the major advantage of the computer is its ability to accurately, rapidly and repeatedly handle complex calculations, a capability already widely used.

The methods adopted by the experimenter for use by the computer are often the same 'desk-top' techniques he is already using, transferred directly to the more powerful machines. They improve the data analysis only by facilitating the calculations and removing, or reducing, operator inaccuracies. In many instances, this represents a gross under-use of the computer's capabilities, since these same properties of speed and accuracy enable a wide range of problem-solving techniques, that require complex repeated calculation, to be applied to pharmacological problems. These methods, the details of which belong to the realms of higher mathematics, find application in many scientific disciplines, and have led to the development of 'easy-to-use' program libraries of the techniques that the mathematically naive, but 'computer competent', user can exploit. This article describes one of the most powerful of these newly available techniques, that of 'curve-fitting', and illustrates how the methods may be applied to pharmacological problems.

Curve-fitting

'Curve-fitting' or more correctly, 'itera-