DISINTEGRINS: A NOVEL FAMILY OF INTEGRIN INHIBITORY PROTEINS FROM VIPER VENOMS

ProductInformation

Disintegrins are a family of cell surface receptors that mediate adhesion with other cells or with extracellular matrix proteins. Interaction with integrins regulates cell adhesion, cell spreading and migration, and change in cell shape. Some integrins have a restricted distribution while others can appear on many different cell types (1). Integrins are composed of a heterodimetric combination of α- and β-subunits. Their interaction with their ligands generally occurs via a common amino acid sequence, Arg-Gly-Asp (RGD), which represents the recognition site.

Disintegrins represent an interesting class of low molecular weight, RGD-containing, cysteine-rich peptides isolated from different snake venoms. They interact with β_1- and β_2-containing integrins, thus preventing their interaction with naturally-occurring ligands. This group represents the most potent known inhibitors of some integrin functions (2,3).

Disintegrins fall into three main subfamilies: a group of short peptides containing 48-49 amino acids and four disulfide bridges (e.g. echistatin), a group of medium-size peptides containing 70-73 amino acids and six disulfide bridges (e.g. flavoridin) and a group of long peptides containing 83-84 residues and seven disulfide bridges. Although disintegrins have a highly conserved RGD recognition site, certain amino acid sequences present in the peptides may modify their activity, specificity, and their ability to compete with various ligands. (2)

Disintegrins may serve as an important tool in basic research due to their various interesting activities. Distegrins specifically bind specifically to the platelet glycoprotein receptor IIb/IIIa. Thus, they are competitive inhibitors of fibrinogen-dependent platelet aggregation induced by ADP, thrombin, epinephrine, and collagen (4,5,6). The quantity required for such inhibition is as low as nanomolar concentration in some models (e.g. kistrin, echistatin). By comparison, the concentration of disintegrins required to cause 50% inhibition of ADP-induced platelet aggregation in platelet-rich plasma was two to three times lower than the required concentration of the short RGDS peptide (6,7). The advantage of disintegrins as potent inhibitors of platelet aggregation in vivo is their short half-life and apparent non-toxicity (5,8). In addition to the activity mentioned, echistatin has been used as a potent inhibitor of bone resportion in cell culture at the nanomolar concentration (9). Other disintegrins inhibit murine melanoma cell metastasis and cell-matrix attachment and cell interaction with fibronectin (7,10,11).

Their interesting activities make disintegrins important tools in basic research. To fill the need for these tools, we have added Echistatin (Product Number E1518), Flavoridin (Product Number F0412), and Kistrin (Product Number K4755) to our Attachment and Matrix Factors product line. Sterile and ninety-five percent pure by SDS-PAGE, they are supplied as gamma-irradiated, Iyophilized products.

Molecular Weights:
E1518 Echistatin MW = 5,000
F0412 Flavoridin MW = 7,500
K4755 Kistrin MW = 7,500

References

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