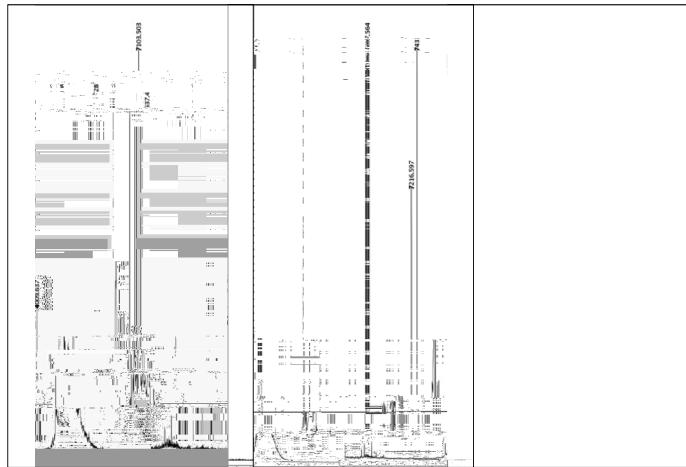


loop containing an RGD, KGD, MVD, MLD, MGD, WGD, VGD, KTS or RTS sequence[10,12e 15]. Although the amino acid residues adja-



after 24 h incubation (both $p < 0.001$; Fig. 6). However, tzabcanin caused only a slight decrease in Colo-205 cell viability at concentrations of 1.75 μM and 3.5 μM (both $p < 0.05$) and at 14 μM

($p < 0.01$); 7 μM tzabcanin also resulted in a decrease in cell survival, but this treatment level failed to reach significance ($p > 0.05$).

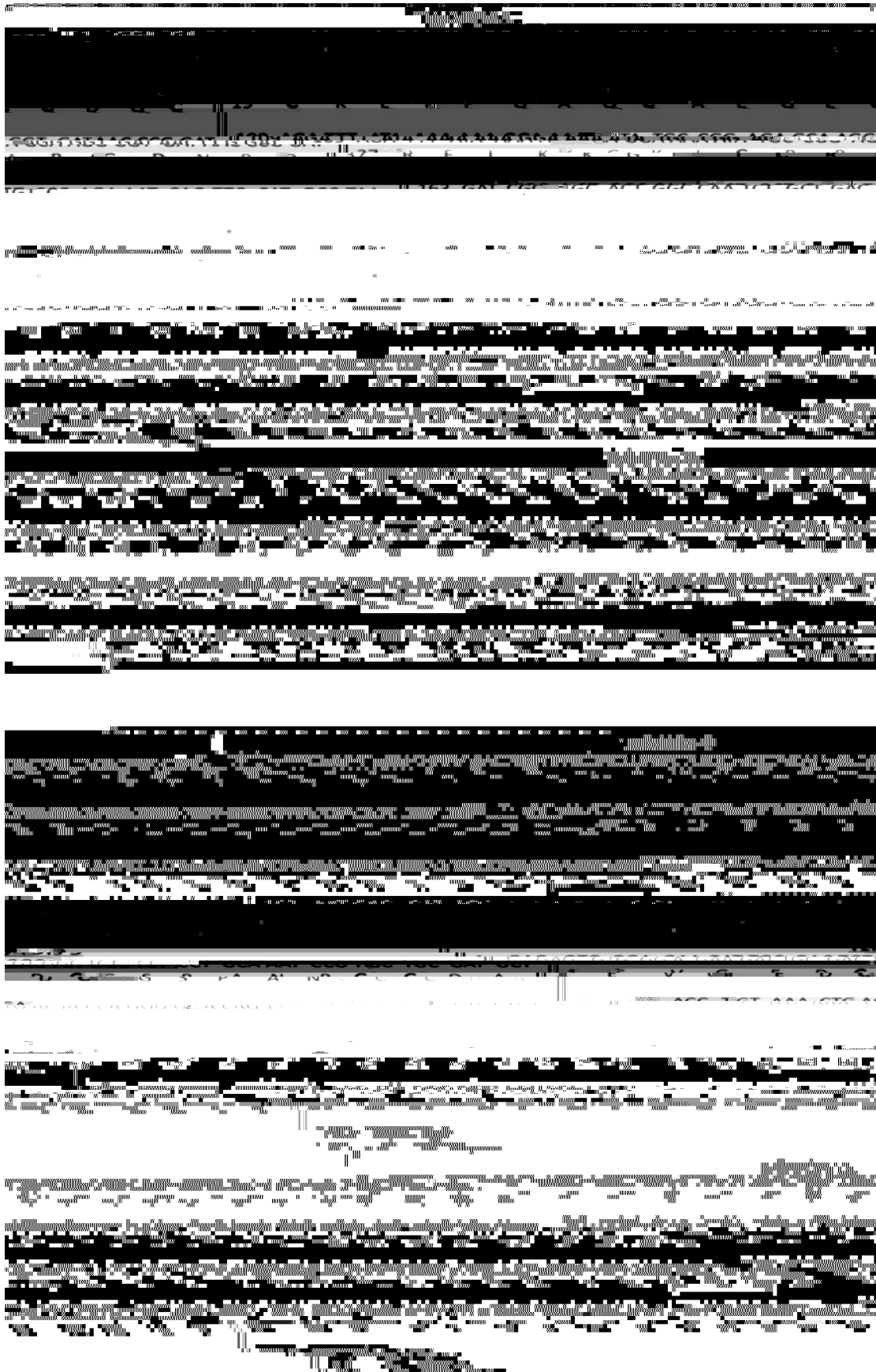


Fig. 4.

high affinity to $\alpha_{11b}\beta_3$ integrins, whereas RGDN show higher selectivity towards both $\alpha_5\beta_1$ and $\alpha_v\beta_3$ integrins [16,17,47]. Of the six disintegrins reported here, four contain an RGDW binding motif, and two, including tzabcanin, contain an RGDN binding region. Yet even with identical integrin-binding regions, structural discrep-

Similarly, the homodimeric disintegrin contortrostatin was found to lack cytotoxicity toward MDA-MB-435 cells *in vitro* [22]. However, recently Lucena et al. [30] showed that recombinant disintegrins r-vidistatin 2 and r-mojastin 1 induced apoptosis in approximately 20% of human pancreatic adenocarcinoma (BXPC-3) cells. Therefore, the slight decrease in Colo-205 cell viability in the presence of high concentrations of tzabcanin could be due to induction of apoptosis, or a loss of membrane integrity, ultimately leading to antiproliferative effects. On the other hand, the potent toxicity of crude venom towards both cell lines is likely due to the presence of LAAOs, SVMPs, and PLAs, which are abundant in *C. s. tzabcan* venom [51] and have been shown to exhibit a combination of cytotoxic and apoptotic activities [52 e 54]. Similarly, Bradshaw et al. [38] also showed that *C. s. tzabcan*

Because many disintegrins have the capability to recognize an array of integrins, the relatively weak potency of tjabcanin suggest that this disintegrin may inhibit cell adhesion by binding to a more select group of integrins, leaving other receptors available for integrin-ECM interactions. Further, tjabcanin also contains an RGDN binding domain which has been shown to exhibit higher affinity to integrin $\alpha_v\beta_3$

[32] M.C. Brown, I. Staniszewska, L. Del Valle, G.P. Tuszynski, C. Marcinkiewicz,