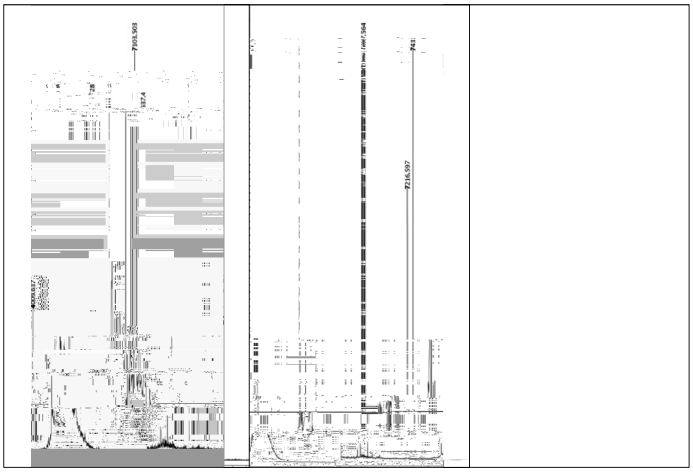
loop containing an RGD, KGD, MVD, MLD, MGD, WGD, VGD, KTS or RTS sequence[10,12 e 15]. Although the amino acid residues adja-



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 mM and 3.5 mM (both $p < 0.05$) and at 14 mM ($p < 0.01$); 7 mM tzabcanin also resulted in a decrease in cell survival, but this treatment level failed to reach signi cance ($p > 0.05$).

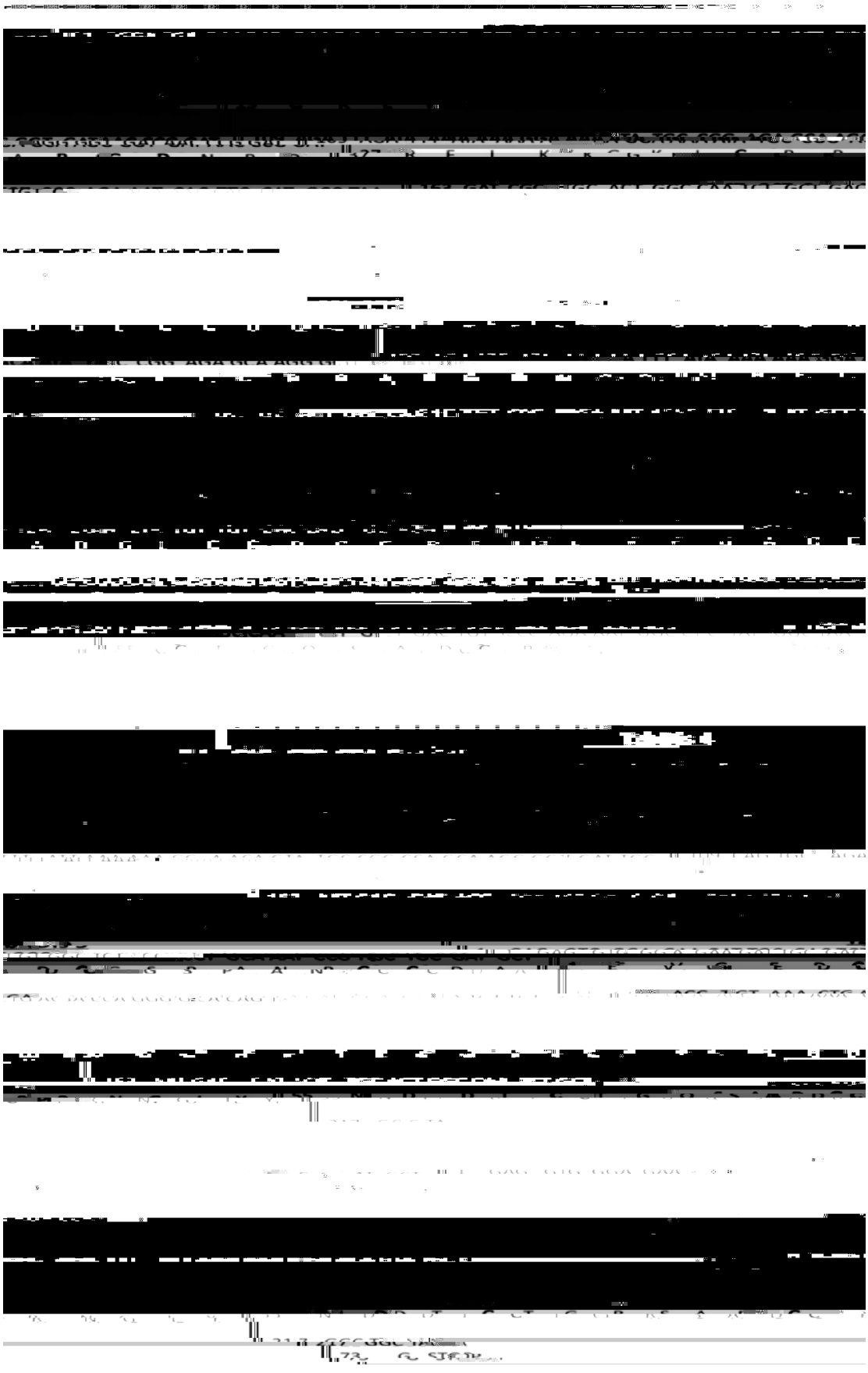


Fig. 4.

high af nity to $a_{IIb}b_3$ integrins, whereas RGDN show higher selectivity towards both a_5b_1 and a_vb_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 discrepancies in the C-terminal region can alter biological activity. Differences in ADP-induced platelet aggregation have been documented between colombistatin and cotiarin, both RGDN disintegrins that differ only by the presence of a Tyr72 in colombistatin, whereas cotiarin exhibits His72 [23].

Although crude C. s. tzabcanvenom was highly toxic to both Colo-205 or MCF-7 cell lines, puri ed tzabcanin showed very low

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-virdistatin 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 PLA2s, which are abundant in C. s. tzabcan venom [51] and have been shown to exhibit a combination of cytotoxic and apoptotic activities [52e54]. 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 tzabcanin 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, tzabcanin also contains an RGDN binding domain which has been shown to exhibit higher af nity to integrin $a_v b_3$

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