عنوان مقاله:

Designing novel teduglutide analogues with improved binding affinity: An in silico protein peptide approach

محل انتشار:

نهمین همایش بیوانفورماتیک ایران (سال: 1398)

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خلاصه مقاله:

Short bowel syndrome (SBS) is a disabling condition with the symptoms characterized by diarrhoea, steatorrhoea, abdominal pain, electrolyte disturbances, dehydration and malnutrition, resulted from the loss of substantial portions of intestine, which leads to inadequate absorption of nutrients and fluids [1-3]. In an effort to help in alleviating symptoms of the condition, the patients in most cases need to receive pharmaceutical treatments. Growth factors and seven other trophic hormones have been used to enhance intestinal adaptation. Human growth hormone, somatropin and L-glutamine have been approved to be used in SBS for short-term usage with limited efficacy [4]. Teduglutide (Gattex, Revestive) is an analogue of GLP-2, which has longer half life compared to GLP-2 due to a single residue substitution. It is the first drug which has been introduced for long-term treatment of SBS with beneficial effects approved in different clinical trials. Teduglutide increases intestinal and portal blood flow, inhibits gastric acid secretion and decreases intestinal motility via binding to the GLP-2 receptors located in intestinal tissue. Human GLP2R has a 173-residue long N-terminal domain which encompasses GLP-2 binding site. The three dimensional (3D) structure of GLP2R hasn't been determined yet. However, the N-terminal domain of its homologous receptor GLP1R complexed with its indigenous ligand GLP-1 has been elucidated using X-ray crystallography. The current study aimed to use computational mutagenesis approach in order to design novel potent analogues of teduglutide.

کلمات کلیدی:

لینک ثابت مقاله در پایگاه سیویلیکا: