Format: Abstract

Biochem Pharmacol. 2015 Sep 15;97(2):203-14. doi: 10.1016/j.bcp.2015.07.033. Epub 2015 Jul 31.

Pharmacological Activities and Hydrolysis by Peptidases of [Phospho-Ser(6)]-Bradykinin (pS(6)-BK).

Assis DM[1], Juliano L[2], Paschoalin T[1], Kouyoumdjian M[3], Calixto JB[4], Santos RA[5], Pertinhez TA[6], Gauthier F[7], Moreau T[7], Blaber M[8], Juliano MA[9].

Author information

Abstract

Phosphorylated kininogen and some of its fragments containing serine phosphorylated bradykinin ([pS(6)]-Bk) were identified in human serum and plasma by a phosphoproteomic approach. We report the kininogenase ability of human tissue and plasma kallikreins and tryptase to generate [pS(6)]-Bk or Lys-[pS(6)]-Bk having as substrate the synthetic human kininogen fluorescent fragment Abz-MISLMKRPPGF[pS(386)]PFRSSRI-NH2. The pharmacological assays of [pS(6)]-Bk showed it as a full B2 bradykinin receptor agonist in smooth muscle, it produces a portal liver hypertensive response in rat and mouse paw edema that lasts longer than Bk. The rat hypotensive response to infusions of Bk is greater than that of [pS(6)]Bk, both if injected through femoral vein or aorta. [pS(6)]-Bk was more resistant than Bk to kininase digestion performed with angiotensin converting enzyme, neprilysin, thimet oligopeptidase, aminopeptidase P and carboxypeptidase M. (1)H-NMR experiments indicated that [pS(6)]-Bk has lower flexibility, with the pS(6)-P(7) bond restricted to the trans conformation, and can explain [pS(6)]-Bk resistance to hydrolysis. In conclusion, [pS(6)]-Bk presenting lower activity than Bk, with longer lasting effects and being slowly released by kininogenases from synthetic Abz-MISLMKRPPGF[pS(386)]PFRSSRI-NH2, suggests that phosphorylation of the kininogens can be an efficient kallikrein-kinin system regulator.

KEYWORDS: Bradykinin (PubChem CID: 439201); Kallikreins; Kinin; Kininogen; Peptidase; Peptides; Protease; Tryptase; [Phospho-Ser(6)]-Bradykinin (PubChem CID: 439201)

PMID: 26235942 DOI: 10.1016/j.bcp.2015.07.033

[PubMed - indexed for MEDLINE]

Publication Types, MeSH Terms, Substances

LinkOut - more resources

PubMed Commons

PubMed Commons home

0 comments

How to join PubMed Commons