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Available online at www.derpharmachemica.com

ISSN 0975-413X
CODEN (USA): PCHHAX

Der Pharma Chemica, 2016, 8(3):235-237
(http://derpharmachemica.com/archive.html)

The role of HPaA protein as candidate vaccine against Helicobacter pylori

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ABSTRACT

Scientists affirmed Helicobacter pylori as strict cause of cancer in humans and type I carcinogen. According to the reports, H. pylori infection occurs in more than half of the world population. Generally H.pylori is accountable for nearby 75% of the entire gastric cancers and 63.4% of the entire stomach cancers over the world. Given the importance of this bacterium and emergence of drug resistant strains need to appropriate vaccine forer abdication of pathogenic strains is felt. The role of UreB, HspA, FlaA, FlaB, CagA, VacA, HpaA as candidate vaccine has been established. For bacterial proteins act as a candidate vaccine antigen, it should preferably be conserved, immunogenic, secreted or surface localized. HpaA protein has all these criteria. According to the conducted studies HpaA protein is a good candidate in the development of vaccines against H. pylori infection, but this factor for inducing appropriate immune responses should be used in combination with the other factors that participating in pathogenesis of infection.

INTRODUCTION

Several approaches to limiting the risk of infections are: 1) inhibition of overgrowth of resident bacteria normally present at low levels in the natural nitch [1], detection and treatment of carrier of opportunistic and pathogenic microorganisms [2, 3] inactivation of microorganisms using nanothechnology [4-7] and photodynamic therapy [8-12], eradication of important healthcare-associated pathogen [13-22] and the use of vaccines that target pathogenic microorganisms. In 1994, scientists affirmed *H. pylori* as strict cause of cancer in humans and type I carcinogen [23, 24]. According to the reports *H. pylori* infection occurs in more than half of the world population and results in gastroduodenal diseases, for example peptic ulcer (about 10%) and gastric adenocarcinoma in about 1–2%. In 2002 year, from expected 1.9 million cases, 17.8% of the global occurrence of cancer, were considered due to infectious diseases, in meantime *H.pylori* infection was considered as the most important cause (5.5% of total cancer cases) [25]. Generally *H.pylori* is accountable for nearby 75% of the entire gastric cancers and 63.4% of the entire stomach cancers over the world [26]. Given the importance of this bacterium and emergence of drug resistant strains need to appropriate vaccine for eradication of pathogenic strains is felt [27]. The role of UreB, HspA, FlaA, FlaB, CagA, VacA, HpaA as candidate vaccine has been established [28]. The close attachment of *H. pylori* to gastric epithelial cells would be considered as the first step in infection, because it may make possible colonization of bacterium, the transportation of effectors proteins like CagA and VacA into eukaryote cells [29]. The continual colonization of the mucous layer of human stomach by *H.pylori* is acquired through multiple factors, which deal with the diverse challenges caused by the unkind environment. It is identified about 20% of *H. pylori* in the stomach is adherent to

the mucus epithelial cells. The bacterium comes into contact with the mucin layer that covers the epithelial cells either by an active or a passive process [30]. The get in touch with the mucin results in a strain-dependent interaction between the mucin and bacterium [31]. *H. pylori* contain six adhesions for sialic acid, of which three genes (*hpa*A, *nap*, *sap*A) have been recognized [31, 32]. Another one is BabA which binds specially to the Lewis B (LeB) antigen in mucin MUC5AC [33]. It has been shown that the first sialic acid adhesion was HpaA [34, 35]. The gene encoding this protein is *hpaA* [34]. The purified form of this protein (~29 kDa) binds to sialoconjugates chiefly in an α 2,3-specific comportment [34, 35]. Nevertheless, in *E. coli*, an expression host for production of recombinant proteins [36], expressing HpaA, hemagglutination activity was not seen, suggesting that the further genes are needed for transfer, assembly, or regulation in process of hemagglutination expression in *H. Pylori*. Moreover, HpaA has as well been observed to be a conserved [35], inner membrane lipoprotein [37], rather than outer membrane protein in *E. coli* [11]. HpaA has also been found that comprising the extracellular flagellar sheath [38]. The outer membrane is a permanent structure on the surface of gram-negative bacteria, which have two-sided particular significance as a possible target for protective immunity in bacterial pathogens [39, 40]. In some studies, outer membrane vaccines have been applied to induce protection against a number of bacteria [41]. For bacterial proteins act as a candidate vaccine antigen, it should preferably be conserved, immunogenic, secreted or surface localized. HpaA protein has all these criteria [42]. The *hpaA* gene is placed in genome DNA of *H. pylori* and noticeably conservative in sequences of nucleotide and amino acid, Furthermore, antibody against HpaA almost could be found in all infected patients sera with *H. pylori*, which will be an ideal antigen candidate for vaccine against *H. pylori* [43]. The necessity of HpaA for bacterial colonization in the gastric mucosa of mice has been shown in 2005 by Elisabet Carlsohn et al, the HpaA mutant strains were not able to creating colonization, and for the first time in vivo a physiological role of HpaA was established [42]. Several studies showed that the *hpaA* gene of the *H. pylori* was a highly conserved prokaryotic gene and might be a possible candidate for *H.pylori* vaccine development [44] although the *hpaA* antigen should be one component of a multiantigenic vaccine [45].

As discussed in study by Mattsson et al the HpaA can increase weakly immune responses after infection in mice, moreover immune responses against HpaA in those with infected *H. pylori* were induced, although poorly [46]. Johanna Nystrom et al assessed H. *pylori* in the stomach after immunization in mice as well as they studied whether the protection might be achieved by mucosal B or T cell or by serum antibody responses after infection, for this, the mice were immunized intragastrically or intraperitoneally, The results have presented that a number of different antigens can inducing a CD4+ T cell response against *H. pylori* and the protection was robustly induced by specific mucosal immune responses, i.e. both CD4+ T cell production and IgA responses [47]. nevertheless, the protective immunity induced by *H. pylori* vaccine including single recombinant antigen was generally limited or only somewhat useful [27, 48]. It is probable that the effective immunity against bacteria could be obtained by combination of different antigens that attributing in many aspects of the pathogenesis, using polyvalent and multicomponent vaccines may be a good strategy for the improvement of *H. pylori* vaccine [27], for example in study performed by X. Huang et al rOmp22–HpaA fusion protein retained immunogenicity and could be used as an antigen candidate in the development of an oral vaccine against *H. pylori* infection [49]. Preventing the stabilization of long-term colonization or even treatment of infections caused by *H. pylori* may be achieved by killing all organisms or by antagonizing one or all of the mechanisms and suppressing growth as long as the combination of the host immune response, exfoliation and the movement of stomach contents eliminate bacteria. Data and information upon prevention of colonization or spontaneous treatment in humans are little; however, there is a number of evidence for both of them, extensive cure of *H. pylori* infection with multidrug therapy is difficult. Therefore, until discover useful vaccines to prevent *H. pylori* infection, improved sanitation and public education may only be appropriate to limiting infection [50].

According to the conducted studies HpaA protein is a good candidate in the development of vaccines against *H. pylori* infection, but this factor for inducing appropriate immune responses should be used in combination with the other factors that participating in pathogenesis of infection.

Acknowledgement
We are grateful to our colleagues in Mashhad University of Medical Sciences for their advices in this work.

REFERENCES

[1] A. Bahador, S. Lesan, N. Kashi, *Iran J Microbiol*, **2012,** 4, 75.
[2] M. Haghighi Hasanabad, M. Mohammadzadeh, A. Bahador, N. Fazel, H. Rakhshani, A. Majnooni, *Iran J Microbiol*, **2011**, 3, 123.
[3] B. Hajikhani, T. Motallebi, J.Norouzi, A. Bahador, R. Bagheri, S. Asgari, L. Chamani-Tabriz, *J Reprod Infertil*, **2013**, 14, 29.
[4] R. Khajavi, MMS. Bahadoran, A. Bahador, A. Khosravi, *J Ind Text*, **2013**, 42, 219.

[5] A. Sodagar, A. Bahador, S. Khalil, A. Saffar Shahroudi, M. Zaman Kassaee, *J Prosthodont Res*, **2013**, 57, 15.
[6] A. Bahador, D. Esmaeili, A. Khaledi, R. Ghorbanzadeh,*J Chem Pharm Res*, **2013**, 5, 65.
[7] A. Bahador, B. Pourakbari, B. Bolhari, FB, Hashemi, *Biomed J*, **2015**, 38, 77.
[8] N. Chiniforush, M. Pourhajibagher, S. Shahabi, A. Bahador, J Lasers Med Sci, **2015**, 6, 139.
[9] N. Moslemi, P. Soleiman-zadeh Azar, A. Bahador, N. Rouzmeh, N. Chiniforush, M. Paknejad, R. Fekrazad, *Lasers Med Sci*, **2014**, 2015, 30, 89.
[10] N. Hakimiha, F. Khoei, A. Bahador, R. Fekrazad, *J Appl Oral Sci*, **2014**, 22, 80.
[11] R. Fekrazad, F. Khoei, N. Hakimiha, A. Bahador, *Photodiagnosis Photodyn Ther*, **2013**, 10, 626.
[12] N. Shamsoulmolouk M. Khayamzadeh , M. Paknejad , G. Poursepanj , MJ. Kharazi Fard, A. Bahador. J Lasers Med Sci. 2016,7, 21.
[13] M.Nasrolahei, B. Zahedi, A. Bahador, H. Saghi, S. Kholdi, N. Jalalvand, D. Esmaeili, *Ann Clin Microbiol Antimicrob*, **2014**, 13, 38.
[14] M. Safari, AS. Mozaffari Nejad, A. Bahador, R. Jafari, MY. Alikhani,*Saudi J Biol Sci*, 22, 424.
[15] J. Moradi, FB. Hashemi, A. Bahador, *Osong Public Health Res Perspect*, **2015**,6, 79. [16] M. Beheshti, M. Talebi, A. Ardebili, A. Bahador, A. Lari, *J Pharm Bioallied Sci*, **2014**, 6, 229.
[17] A. Bahador, R. Raoofian, M. Taheri, B. Pourakbari, Z. Hashemizadeh, FB. Hashemi, *Microbial Drug Resistance*, **2013**, 20, 632.
[18] A. Bahador, M. Taheri, B. Pourakbari, Z. Hashemizadeh, H. Rostami, N. Mansoori, R. Raoofian, *Microbial Drug Resistance*, **2013**, 19, 397.
[19] M. Safari, M. Saidijam, A. Bahador, R. Jafari, MY. Alikhani, *J Res Health Sci*, **2013**, 13, 162.
[20]A. Bahador, R. Raoofian, B. Pourakbari, M. Taheri, Z. Hashemizadeh, FB. Hashemi. *Front Microbiol*.**2015,** 13, 1249. doi: 10.3389/fmicb.2015.01249.
[21] Z. Farshadzadeh, FB. Hashemi, S. Rahimi, B. Pourakbari, D. Esmaeili, MA. Haghighi, A. Majidpour, S. Shojaa, M. Rahmani, S. Gharesi, M. Aziemzadeh, A. Bahador. *Front Microbiol*. **2015** 20, 1146. doi: 10.3389/fmicb.2015.01146.
[22] A. Bahador, R. Raoo An, Z. Farshadzadeh, L. Beitollahi, A. Khaledi, S. Rahimi,
M. Mokhtaran, A. Mehrabi Tavana, D. Esmaeili. *Jundishapur J Microbiol*. **2015**,27, e17167. doi: 10.5812/jjm.17167v2.
[23]DM. Parkin, F. Bray, J. Ferlay, P. Pisani. *CACancer J Clinicians*. **2005**, 55, 74.
[24] J. Khatoon, RP. Rai, KN. Prasad. *World J Gastrointest Oncol*. **2016**, 15, 147.
[25] T. Ohkusa, K. Fujiki, I. Takashimizu, J. Kumagai, T. Tanizawa, Y. Eishi, et al. *Ann Intern Med*. **2001**,134,380.
[26] Y. Niv. *World J Gastroenterol*. **2008**, 14, 1477.
[27] RX. Tang, DJ. Luo, AH. Sun, J. Yan. *World J Gastroenterol*. **2008**, 14, 4816.
[28] S. Odenbreit. *Int J Med Microbiol*. **2005**, 295, 317.
[29] H. Yoshiyama, H. Nakamura, T. Okamoto, K. Okita, T. Nakazawa. *Aliment Pharmacol Ther*. **2000**, 14, 230.
[30] T. Wadstrom, S. Hirmo, T. Boren. *Aliment Pharmacol Ther*. **1996**, 10, 17.
[31] TL. Testerman, DJ. McGee, HL. Mobley. *J Clin Microbiol.* **2001**, 39, 3842.
[32] JH. Van de Bovenkamp, J. Mahdavi, KV. Male, M. Anita, HA. Büller, AW. Einerhand, et al. *Helicobacter*.**2003**, 8, 521.
[33] D. Evans, T. Karjalainen, D. Evans, D. Graham, CH. Lee. *J Bacteriol*. **1993**, 175, 674.
[34] DG. Evans, D. Evans, JJ. Moulds, DY. Graham. *Infect Immun*. **1988**, 56,2896.
[35] J. Yan, YF. Mao, ZX. Shao. *World J Gastroenterol*. **2005**, 11, 421.
[36]S. Mahmoudi, H. Abtahi, A. Bahador, G. Mosayebi, AH. Salmanian, *Pak J Biol Sci*, **2010**, 13, 380.
[37]PW. O'Toole, L. Janzon, P. Doig, J. Huang, M. Kostrzynska. *J bacteriol*. **1995**, 177, 6049.
[38] KH. Valkonen, T. Wadström, AP. Moran. *Infect Immun*. **1997**, 65, 916.
[39] RA. Alm, J. Bina, BM. Andrews, P. Doig, RE. Hancock. *Infect Immun*. **2000**, 68, 4155.
[40] JI. Keenan, RA. Allardyce, PF. Bagshaw. *FEMS Microbiology letters*. **1998**, 161, 21.
[41] X. Liu, J. Hu, X. Zhang, D. Fan. *Chinese Med J*. **2002**, 115, 1513.
[42] E. Carlsohn, J. Nyström, I. Bölin, CL. Nilsson, AM. Svennerholm. *Infect Immun*. **2006**, 74, 920.
[43] AC. Jones, R. Logan, S. Foynes, A. Cockayne, BW. Wren, CW. Penn. *J Bacteriol*. **1997**, 179, 5643.
[44]DG. Evans, TK. Karjalainen, DJ Jr. Evans, DY. Graham, CH. Lee. *J Bacteriol*. **1993**, 175, 674.
[45] P. Sutton, C. Doidge, G. Pinczower, J. Wilson, S. Harbour, A. Swierczak, et al. *FEMS Immunol & Med Microbiol.***2007**, 50, 213.
[46] A. Mattsson, A. Tinnert, A. Hamlet, H. Lönroth, I. Bölin, AM. Svennerholm. *Clin Diagn Lab Immunol*. **1998**, 5, 288.
[47] J. Nyström, AM. Svennerholm. *Vaccine*. **2007**, 25, 2591.
[48] B. Sun, ZS. Li, ZX. Tu, GM. Xu, YQ. Du. *World JGastroenterol*. **2006**, 12, 7042.
[49] X. Huang, B. Xu, G. Duan, C. Song. *Current microbiology*. **2013**, 67**,** 487.
[50] H. Brenner, G. Berg, N. Lappus, U. Kliebsch, G. Bode, H. Boeing. *Epidemiology*. **1999**, 10, 214.