Stable Gastric Pentadecapeptide BPC 157

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Stable gastric pentadecapeptide BPC 157 especial therapy effects combine the therapy of myocardial infarction, heart failure, pulmonary hypertension arrhythmias, and thrombosis prevention and reversal. The shared therapy effect occurred as part of its even larger cytoprotection (cardioprotection) therapy effect (direct epithelial cell protection; direct endothelium cell protection) that BPC 157 exerts as a novel cytoprotection mediator, which is native and stable in human gastric juice, as well as easily applicable.

stable gastric pentadecapeptide BPC 157 | peptide therapy | hearth disturbances

1. Introduction

Numerous key clinical trials published or presented at major international conferences over the course of 2021 were reviewed as the most valuable contributions to clinical cardiology (for review, see, i.e., [1]). Heart failure data focused on trials with sodium–glucose cotransporter 2 (SGLT2) inhibitors, sacubitril/valsartan, and mavacamten for hypertrophic cardiomyopathy [1]. Proprotein convertase subtilisin/kexin type 9 (PCSK9) inhibitors were centered in the prevention trials [1].

On the other hand, as a new attempt, from the cytoprotection viewpoint and potential involvement of the cytoprotective agents, authors reviewed the potential significance in the heart disturbances of the therapy with the stable gastric pentadecapeptide BPC 157 (for review, see, i.e., [2][3][4][5][6][7][8][9]). It appeared, as a peptide native and stable in human gastric juice, as a late outbreak of the cytoprotection/organoprotection concept of Robert and Szabo, a concept mostly from the stomach studies [10][11][12][13][14][15][16][17] for epithelial and endothelial protection, like the previous theoretical/practical breakthroughs in the 1980s and brain–gut axis and gut–brain axis (for review, see, i.e., [2][3][4][5][6][7][8]). However, its compelling basic highlights (particular vascular effect, activation of the collateral pathways) [18][19][20][21][22][23][24][25][26][27][28][29][30][31][32][33][34][35][36][37][38][39][40][41] in the most valuable animal models might still need confirmation as the vast clinical evidence obtained in the huge number of clinical trials [1]. Nevertheless, it might challenge further therapy use.

2. Cytoprotection Background (Direct Epithelial Cell Protection) for BPC 157 Beneficial Activity

The wide applicability of the original postulates of Robert and Szabo's cytoprotection concept (for review, see, i.e., [10][11][12][13][14][15][16][17]) might approach the entire problem of heart failure. This wide approach might be useful as a large number of the concomitant diseases with heart failure might be the key for the therapeutic effects [42][43][44], as the stable gastric pentadecapeptide BPC 157 pleiotropic effect belongs to the cytoprotective class of agents (for review, see, i.e., [2][3][4][5][6][7][8]). Note the general background of the BPC 157 beneficial effects on various organs injuries (for review, see, i.e., [2][3][4][5][6][7][8]), which helps one recognize the wide significance of the cytoprotection concept of Robert's (direct epithelial cell protection) [10] and Szabo's (direct endothelium cell protection) [12] that is initiated in the stomach to be further generalized. The foundation of the cytoprotective agents' putative activities in the stomach studies was the initial basic point for their possible therapy extension [10][11][12][13][14][15][16][17]. In general, BPC 157 successfully follows the common cytoprotective principle: the original cytoprotective agent with a prime beneficial effect in the stomach (direct (epithelial) cell protection) had to be transmitted to similar beneficial effect in other organ lesions as well (cytoprotection → organoprotection) [10][11][12][13][14][15][16][17] (for review, see, i.e., [2][3][4][5][6][7][8]). Noteworthily, BPC 157 therapy, in practical terms (native and stable in human gastric juice for more than 24 h, and, thereby, easily applicable), unlike standard cytoprotective agents, fully presumes original cytoprotective requirements (for review, see, i.e., [2][3][4][5][6][7][8]). Thereby, the extent of the obtained beneficial effects largely overrides the range of the beneficial effects commonly reported with the standard cytoprotective agents (for review, see, i.e., [2][3][4][5][6][7][8]) (i.e., prostaglandins' beneficial effects on stomach [10], intestine [13], liver [45], pancreas [13], kidney [46], and heart [47]). Unlike the effectiveness only given before injury (prophylactic effect) of the standard cytoprotective agents (for review, see, i.e., [10][11]), BPC 157, in addition to its prophylactic effect, has a strong curative effect given even much later after injury induction, during ischemia as well as during reperfusion (for review, see, i.e., [2][3][4][5][6][7][8]). Illustratively, as mentioned before, in the vascular studies, as a part of the severe vascular and multiorgan failure syndrome counteraction, there was counteraction of the brain, heart, lung, liver, kidney, and gastrointestinal lesions [18][19][23][24][27][28][29][31][37][38][39][40]. Moreover, in other separate studies, there was counteraction of the brain [48], spinal cord [35][36], heart failure [49], lung [41][50][51][52], liver lesions [53][54][55], liver, gastrointestinal and brain lesions [56][57][58][59][60][61], and kidney [62][63][64] and pancreas [65][66] lesions. There was also a strong wound-healing effect (for review, see, i.e., [3][67]). Thereby, there was the curing of the skin [68][69][70][71][72], nerve [73], tendon [74][75][76][77][78][79][80], muscle [79][80][81][82][83][84], ligament [85], and bone [86][87][88] injuries that spontaneously might not heal. In particular, there was a capability to simultaneously organize the healing of the different tissues (as an example occurred the healing of the osteotendinous junction [77][78] and the healing of the myotendinous junction [80] (and neuromuscular junction function recovering [89]) or the healing of the fistulas, external and internal [90]). Likewise, in particular regard for wounding [3][67], these realized healing effects in the various wounds [68][69][70][71][72][73][76][77][78][79][80][81][82][83][84][85][86][87][88][90] might evidence the realized healing process after blood vessel are ruptured as a whole, and thereby, as we claimed [91], a distinctive effect on all four major events in clot formation and dissolution was fully accomplished. This meant a highly utilizable special effect, especially with heart failure therapy [18][19][23][24][27][28][29][31][37][38][39][40]. Moreover, BPC 157 is very safe, with no adverse effect in clinical trials (i.e., ulcerative colitis), and lethal dose (LD1) was not achieved in toxicology studies (for review, see, i.e., [2][3][4][5][6][7][8]).

Thereby, these beneficial effects (for review, see, i.e., [2][3][4][5][6][7][8]) fulfill the cytoprotection (organoprotection) frame at the general level (implied direct cell protection) [10][11][12][13][14][15][16][17], with all of the mentioned beneficial effects as pre-requests for the resolved heart disturbances. In these terms, the effect on the heart (cardioprotection) might be an additional part of the cytoprotective activity (for review, see, i.e., [10][11][12][13][14][15][16][17][92][93][94]), and, in particular, it might be commonly taken as proof and consequence of its innate cytoprotective activity (for review, see, i.e., [2][3][4][5][6][7][8]). In addition to being native and stable in human gastric juice for more than 24 h, BPC 157 was found in situ hybridization and immunostaining studies in humans to be largely distributed in tissues [3][67] and may have additional physiologic regulatory roles [8][67] as it is thought to be a novel cytoprotective mediator. Furthermore, there is a particular healing effect depending on the tissue involved (for review, see, i.e., [3][67]). Particularly, there is an improved healing effect (for review, see, i.e., [3][67]) for eye injuries (no angiogenesis) [95] versus advanced angiogenesis in other tissues (i.e., tendon, muscle) [79] (for review, see, i.e., [3][67]), which together might provide evidence that BPC 157s beneficial effect is even more complex and tissue specific. Illustratively, BPC 157 eye drops successfully closed perforating corneal incisions in rats; controls developed new vessels that grew from the limbus to the penetrated area, whereas BPC 157-treated rats generally had no new vessels, and those that did form in the limbus did not make contact with the penetrated area [95]. Thus, important for heart healing as well, BPC 157 certainly might control one of the most important aspects of the cytoprotection and cytoprotective agents activity in long terms (i.e., days): the angiogenesis (corneal avascularity as “angiogenic privilege”) (for review, see, i.e., [3][67]).

3. Cytoprotection Background (Direct Endothelial Cell Protection) for BPC 157 Beneficial Activity

Overwhelmingly focused on stomach cytoprotection, the pioneers, Robert (direct epithelial cell protection) [10] and Szabo (direct endothelium cell protection) [11], estimated in stomach damage studies the maxim endothelium maintenance → epithelium maintenance as rapid injury, rapid defensive response, vascular injury within less than 1 min, thrombus and stasis [11], thereby, although not claimed, Virchow triad circumstances. Moreover, finally, the rapid recovery of damaged endothelium occurred as a shared effect of the cytoprotective agents within stomach cytoprotection [11]. With BPC 157 effect (see above), there is an advanced practical realization of the original maxim functioning [8]. This might be the rapid upgrading of the minor vessel to take over the function of the disabled major vessel [18][19][23][24][27][28][29][31][37][38][39][40], as the particular effect on the vessel relied on the given injury. Furthermore, this implies competing with the Virchow triad circumstances devastatingly present, making possible the recruitment of collateral blood vessels, compensating vessel occlusion, and reestablishing blood flow or bypassing the occluded or ruptured vessel [18][19][23][24][27][28][29][31][37][38][39][40]. Illustrative examples might be the therapy of glaucoma in rats after the cauterization of three of the four episcleral veins [26], venous congestion, and the increased intraocular pressure and consequent glaucoma injurious course [26]. For the BPC 157 therapy importance estimation [18][19][23][24][27][28][29][31][37][38][39][40], one remaining episcleral vein was upgraded so that BPC 157 therapy did compensate all functions; otherwise, inescapable venous congestion and the increased intraocular pressure and consequent glaucoma injurious course fully reversed [26]. Moreover, BPC 157 therapy (the rapid upgrading of the collateral pathways) has cured many severe syndromes, including multiorgan and vascular failure

[18][19][23][24][27][28][29][31][37][38][39][40], and heart dysfunction and thrombosis as cause–consequence, in particular. Otherwise, without therapy, these syndromes were commonly presented in rats with the permanent occlusion of major vessels (veins and/or arteries [18][19][20][22][23][24][25][26][27][28][29][30], peripherally and centrally), major intoxication (lithium, alcohol) [39][40], acute pancreatitis [37], myocardial infarction [37], and maintained intra-abdominal hypertension [31]. Its applicability in the rapid upgrading of the collateral pathways may likely provide an additional beneficial effect for the heart functions, and various vessel tributaries, and normalization/attenuation of the intracranial (sinus sagittal) hypertension, portal and caval hypertension and aortal hypotension, and counteraction of the multiorgan failure syndrome [18][19][23][24][27][28][29][31][37][38][39][40].

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