TRANSLATIONAL ASPECTS OF PLACE OF HYDROGEN SULFIDE-RELEASING NON-STEROIDAL ANTI-INFLAMMATORY DRUGS ON THE TOMORROW'S LANDSCAPE FOR STRESS-ASSOCIATED DISORDERS

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Non-steroidal anti-inflammatory drugs (NSAID) are ones of the most widely prescribed drugs in medicine and up-to-date data have expanded their therapeutic role into complex biological processes such as oncogenesis, tissue repair, and different disorders related to aging, despite of dangerous adverse effects which can be fatal (gastrointestinal (GI) bleeding etc). Latest extensive research of multifunctional activities of hydrogen sulfide (H_2S) has proven its potent cytoprotective and vasoprotective, as well as anti-inflammatory effects and developed background of introduction novel NSAID-H_2S-releasing moiety compounds (NSAID-H_2S). Different NSAID-H_2S were created and tested in multicentral investigations (Wallace, 2007-2017) recently.

According to modern views and 11th Revision of International Statistical Classification of Diseases and Related Health Problems (ICD 11), stress is a major pathophysiological factors in several visceral pathologies, including stress-associated GI diseases (SAGID), as stress-associated gastritis, duodenitis, stress-induced ulcer of gastric or duodenal mucosa, therefore, development of effective and safe anti-stress therapies remains an urgent priority. Since histologically stress-associated damage in SAGID look similar, we also predicted that the GI mucosal defence might be also improved by stimulating anti-inflammatory and vasotropic activities. angiogenesis.

In our sets of experiments we tested our hypothesis that NSAID-H_2S: hydrogen sulfide-releasing derivative of naproxen (H_2S-naproxen, ATB-346) and hydrogen sulfide-releasing derivative of aspirin (H_2S-aspirin, ATB-340) vs classical NSAID may results on GI cytoprotective activity. Pre-treatment of NSAID-H_2S in both (single and 2 weeks) administration against stress-related injury inducted by water immersion restricted stress model (Takagi, 1964) results in potent cytoprotective and anti-inflammatory effects which were estimated by histomorphological analysis on esophageal, gastric, intestinal mucosa in the animal models of SACID and serological level of VCAM-1, IL-6 by ELISA. We reviewed here similar and differential age-depended actions of ATB-340 on gastric mucosal defence too. Our recent data also indicate that expression of stress-associated damage was decreased in mesenterium during administration of ATB-340. Hence, NSAID-H_2S are potent, based on endogenously derived agents (stimulation H_2S and elimination cyclooxygenase activities), which are directly associated with mucosal defence against stress injury, in which inflammation seems to be the most important process, they are promised drugs in short future for SAGID treatment after clinical trials.