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## Co-transmission by nitric oxide, substance P and acetylcholine in the pathophysiology of diabetic gastroparesis

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The aims of the study is to investigate the role of Nitric Oxide (NO), Substance P (SP) and AcetylCholine (ACh) in the pathogenesis and to evaluate the effectiveness of existing drugs on the treatment of diabetic gastroparesis. Computer model of a muscle fiber connected to a ganglion, and a segment of the human stomach based on morphostructural, biochemical and physiological data, obtained from *in vivo* and *in vitro* experiments, were developed. Diabetic gastroparesis was reproduced by altering levels of NO and SP in the system. NO acting alone has hyperpolarized the smooth muscle membrane, decreased the amplitude and increased the frequency of slow waves, and abolished action potentials. However, application of prokinetic drugs restored the spiking activity and motility in the segment at reduced frequency and amplitude compared to the norm. SP and ACh release conjointly caused a prolonged depolarization and tonic contraction of smooth muscle. The combined effects of SP, ACh and NO on the segment was decreased in the resting membrane potential, preservation of slow waves and the development of low intensity phasic contractions. Further treatment with prokinetic drugs abolished slow waves and spikes, and induced long-lasting contractions. The model quantitatively and qualitatively reproduced electrical and mechanical patterns of activity of the normal, adynamic, and pharmacologically modulated stomach. Multiple neurotransmission and respective receptor polymodality are the main contributing factors, while each neurotransmitter per se plays a limited role in pathogenesis of diabetic gastroparesis. Erythromycin and metoclopramide do not restore motility and “worsen the paralysis”. Co-localization and co-transmission by multiple neurotransmitters should be taken into consideration when new drugs to treat diabetic gastroparesis are designed.

### Biography

Roustem N Miftahof is the Director of Computational Biology and Medicine Centre at Arabian Gulf University, Manama, Bahrain. He has published numerous books and more than 150 papers in peer-reviewed international journals and has been invited to give speeches at international congresses, conferences and meetings worldwide.

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