EFFECT OF BPTU, AN ALLOSTERIC ANTAGONIST OF THE P2Y1 RECEPTOR, ON THE PURINERGIC RELAXATION OF THE RAT GASTROINTESTINAL TRACT

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INTRODUCTION

Gastrointestinal motility is the result of the coordinated action of smooth muscle cells (SMC), neurons of the enteric nervous system and interstitial cells of Cajal[1]. The principal neurotransmitters of inhibitory motor neurones are nitric oxide (NO) and ATP, which produce SMC relaxation[1,2,3,4]. The receptor P2Y1 is responsible for purinergic relaxations[5,6].

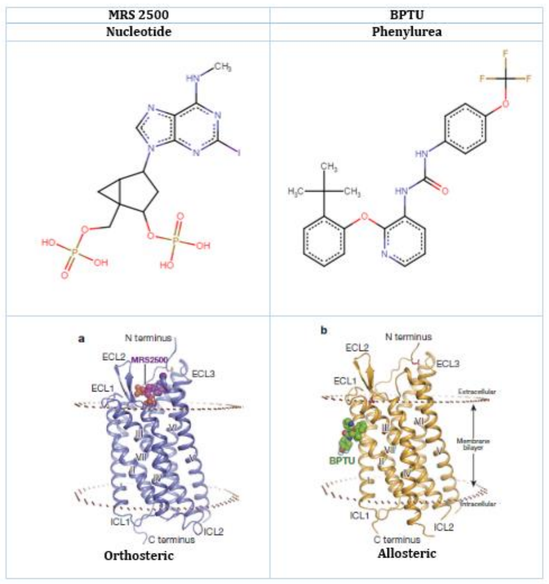

***Figure 1. Comparison MRS2500 vS. BPTU**. Information obtained from Zhang et al. (2015) and Guide to Pharmacology (IUPHAR/BPS) (Pawson et al., 2014).*

OBJECTIVE AND JUSTIFICATION

The aim of this study was to characterize the effect of a new antithrombotic drug named BPTU on purinergic relaxations of the rat gastrointestinal tract. BPTU is the first allosteric antagonist of the P2Y1 receptor.

MATERIAL AND METHODS

The study was performed with 10 rats Sprague Dawley (5 males and 5 females). Circular oriented muscle strips from colon and antrum were studied using the organ bath technique (NANC conditions and L-NNA).

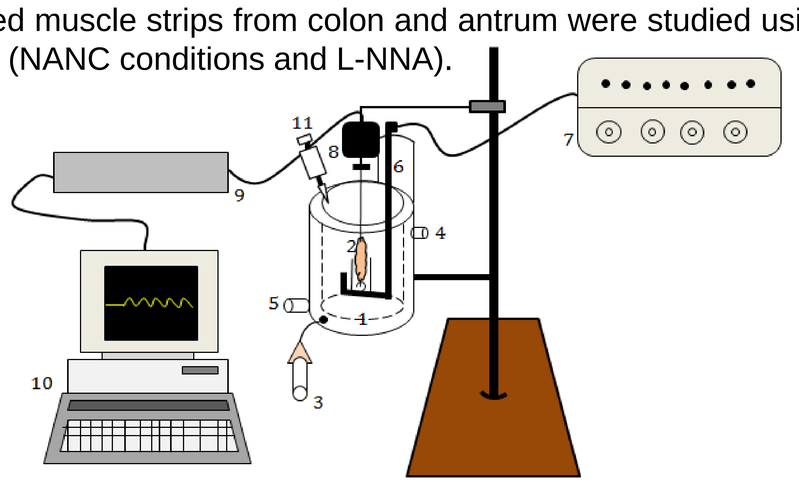

***Figure 2. Diagram of organ bath**. 1. Cup (10 ml); 2. Preparation of circular smooth muscle; 3. Entry of carbogen; 4 and 5. Entry and exit of warm water (37ºC) 6. Electrode; 7. Stimulator; 8. Isometric transducer; 9. A / D converter; 10. Computer; 11. Addition of exogenous drugs.*

RESULTS

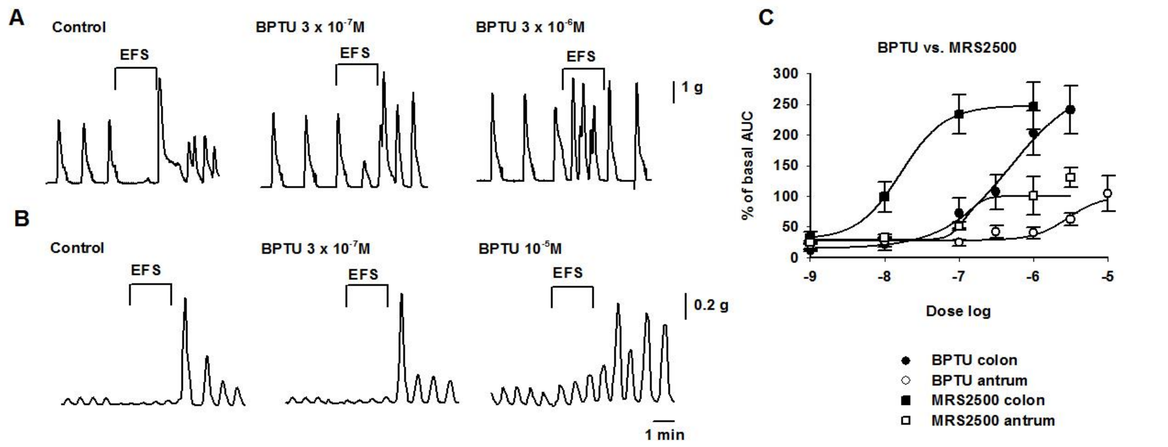

***Figure 3**. **Effect of BPTU on purinergic relaxation in the rat gastrointestinal tract**. Both orthosteric (MRS2500) and allosteric (BPTU) antagonists blocked the relaxation in a concentration-dependent manner. MRS2500 was more potent than BPTU. The antrum needed more concentration than the colon in both antagonists.*

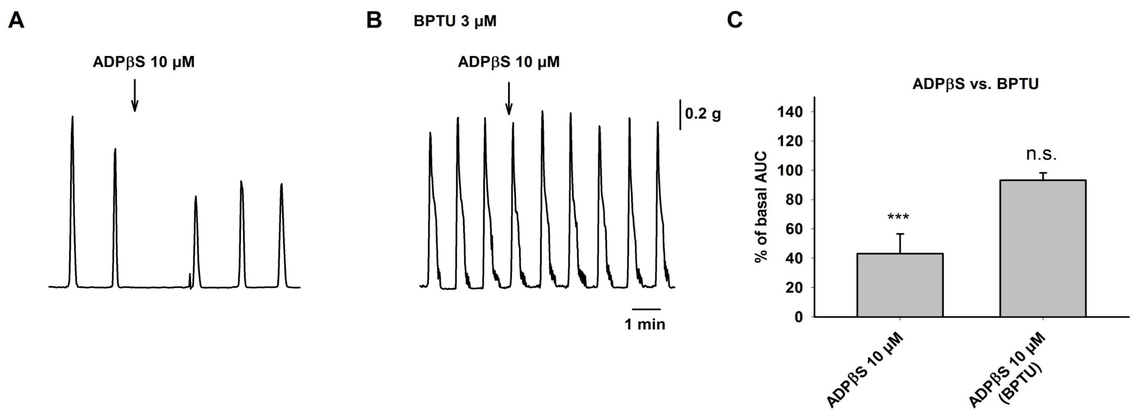

***Figure 4. Effect of BPTU on the purinergic relaxation induced by ADPβS in rat colon**. BPTU blocked the relaxation produced by ADPβS (P2Y1 agonist).*

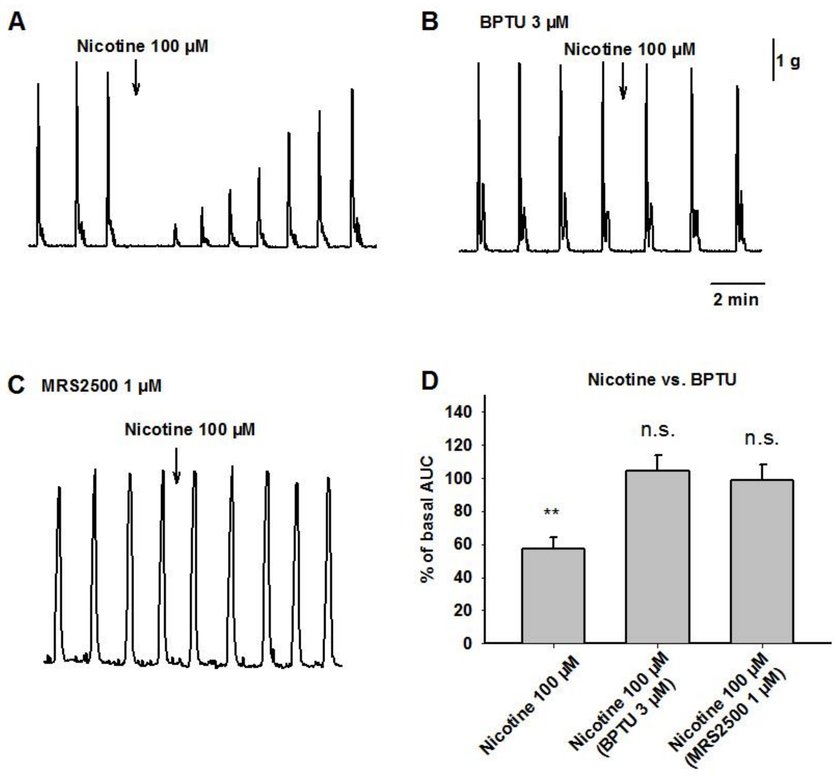

***Figure 5**. **Effect of BPTU on relaxation induced by nicotine in the rat colon**. BPTU and MRS2500 blocked in a concentration-dependent manner the relaxation induced by nicotine.*

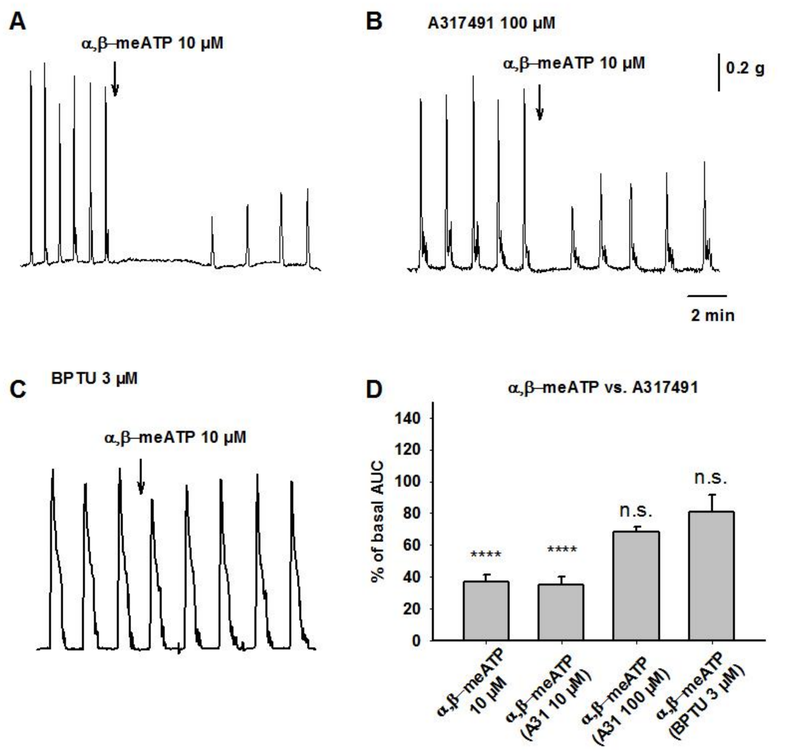

***Figure 6**. **Involment of P2X receptors in purinergic relaxation.** A317491 (selective antagonist of P2X3 receptor) and BPTU blocked the relaxation produced by α,β-methylene-ATP (P2X agonist).*

DISCUSSION

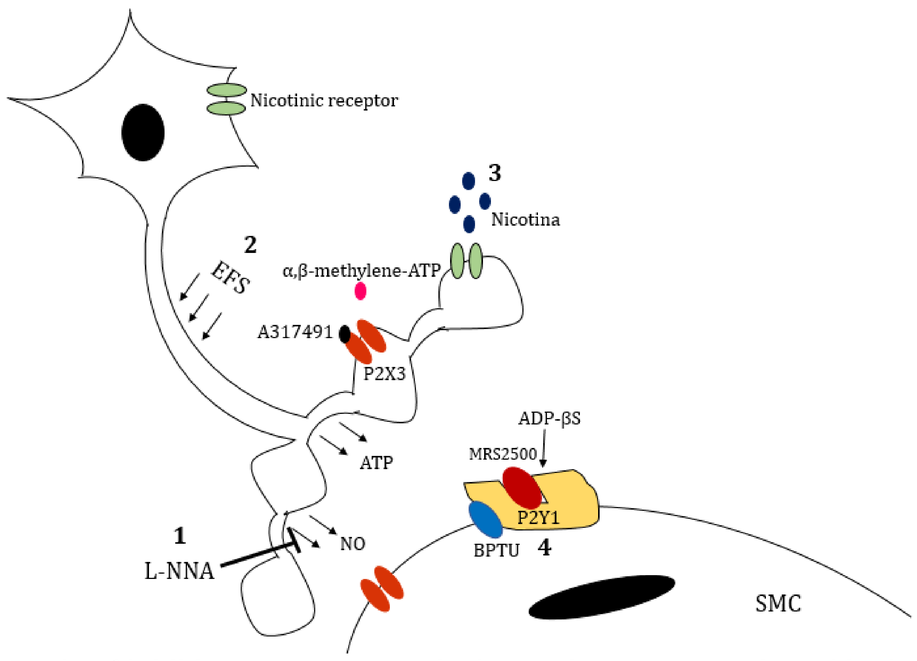

Figure 7. Basis of inhibitory neurotransmission and concepts reviewed in the study

CONCLUSION

BPTU reverses the purinergic relaxation in rat gastrointestinal tract. It is a possible side effect to consider when used as an antithrombotic. Furthermore, their use can be considered as a treatment for motor digestive diseases to increase the gastrointestinal motility.

The results of this study will be published in the paper: BPTU, an allosteric antagonist of P2Y1 receptor, blocks nerve mediated inhibitory neuromuscular responses in the gastrointestinal tract of rodents.

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