## COMMENT ON: USE OF ANKAFERD BLOOD STOPPER FOR CONTROLLING ACTIVELY BLEEDING FUNDAL VARICES

Dear Sir.

We read with interest the recent case report by Okten et al<sup>(1)</sup> showing the successful haemostatic effects of Ankaferd Blood Stopper (ABS) in a patient with fundal variceal haemorrhage. In their report, the authors proved the efficiency of this novel haemostatic agent, even in patients with gastrointestinal bleeding (GIB) due to fundal varices. They concluded that in serious bleeding gastric fundal varices, ABS can act as a bridge in the absence or unavailability of definitive therapies. In addition to the proposed mechanisms of ABS in GIB, we would like to draw attention to a possible underlying mechanism for this antihaemorrhagic effect of ABS, which we think is important in interpreting their results.

As already mentioned by the authors, the most well-known mechanism of action of ABS is promoting the formation of an encapsulated protein mesh that acts as an anchor for erythrocyte aggregation without significantly interfering with individual coagulation factors. (2,3) Although this proposed mechanism is noteworthy in several respects, there is a growing body of evidence suggesting the role of ABS in cellular apoptotic response modulation to haemorrhagic stress, as well as its haemostatic haemodynamic activity. (4) Apart from erthyrocyte aggregation, ABS has many effects on proteins in the tissue and blood, leading to dose-dependent reversible protease-activated receptor (PAR)-1 down-regulation. A sustained PAR-1 down-regulation in the presence of lipopolysaccharides is induced by ABS. These findings are compatible with other investigations focusing on the endothelial haemostatic molecules, EPCR and PAI-1. ABS may act as a topical biological response modifier with anti-haemorrhagic actions. (5) Moreover, ABS-induced formation of the protein network has several essential components. Vital erythroid aggregation takes place in conjunction with the spectrin and ankyrin receptors on red blood cell membranes. Essential erythroid proteins (cyclic AMP response element-binding protein, actin-depolymenisation factor, ankyrin recurrent and FYVE bundle containing protein 1, interferon-stimulated response element, spectrin alpha, actin-depolymerising factor, mitochondrial NADP<sup>[+]</sup> dependent malic enzyme) are included in the protein library of ABS. These regulator molecules affect distinct steps of cellular proliferation such as cell vascular haemostasis, angiogenesis, signal transduction, apoptosis, inflammation, acute phase reaction and several metabolic molecular pathways. ABS also upregulates the GATA/FOG transcription system, which affects erythroid functions and urotensin II. (6) Urotensin II is also an essential component of ABS and acts as a link between active erythroid cells, adhesive proteins and injured vascular endothelium. (5-7)

In conclusion, ABS could have an efficient place for the 'difficult-to-manage' subtypes of gastrointestinal bleedings. ABS may serve as an adjuvant and/or primary agent for these situations, even in patients with variceal haemorrhage.

Yours sincerely,
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Editor's Note: The authors, Okten et al, have declined to comment on the above letter.

