Regarding "Haemolytic Effects of Hypo-osmotic Salt Solutions on Human Erythrocytes" in *Kathmandu University Medical Journal* 2011;34(2):35-9.

Dear Editor of KUMJ

I wish to write a comment regarding the article entitled "Haemolytic Effects of Hypo-osmotic Salt Solutions on Human Erythrocytes" published in April-June Issue of KUMJ in 2011.

Our paper published in KUMJ has attracted a wide readership.[1] According to research gate, more than 800 people have read our article. In view of such interest, I tried to understand the possible mechanism responsible for observation that hypotonic salt solutions of potassium are more effective than the sodium salt solutions of similar strengths, in hemolysing human red blood cells. Could it be a Hofmeister Effect? A search of pertaining literature revealed that a century ago Hofmeister[2] found that sodium salts were better than potassium salts in precipitating the proteins from milk! Protein stability and enzymatic activity seem to be affected by ions.[3-5] Several hypotheses were put forward to explain the 'Hofmeister Effect' but none of them were found to be completely satisfactory.[6] The process of hypotonic hemolysis involves participation of several cyto-skeletal proteins like actin, spectrin, ankyrin and band 3 proteins which are involved in the swelling of red cells, assumption of spherical shape, formation of holes in the membrane through which hemoglobin escapes, leaving a ghost cell.[7-9] Differing affinities of sodium and potassium for one or more of these proteins is most likely to be responsible for the differences that is reported in the paper. Further work is needed to confirm that the findings are indeed due to a Hofmeister effect.

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Dear Sir,

Thank you for your interesting comment in our article. Indeed, our paper has attracted a wide readership in research gate.[1] As rationalized, the role of 'Hofmeister Effect' in this study, demonstrated by ions in hemolysis of red cells, for precipitation of cytoskeletal proteins, cannot be ignored and, must be coupled with further scientific experimental work to put forward the evidence based conclusion. It would be quite interesting to elucidate the mechanism of potassium ion on the red cell membrane in hypo-osmotic solution that may have unexplained cell volume regulatory function in the plasma osmolarity in physiological range. Moreover, the findings of further work may hold the key to the understanding of potassium ion effect on cell volume regulation. Because, exposure of any eukaryotic cells to anisotonic fluid also alters the volume of intracellular organelles such as mitochondria. There has been recent updates on declined efficiency of mitochondrial function for production of ATP despite normal oxygen tension in diabetics. It is conjectured that the fall in plasma osmolarity caused by pathophysiological phenomenon in a diseased state, with normal potassium concentration in plasma, may have deleterious and a threatened effect on cell volume regulation of the body tissues as a whole. It is not possible to pen down the scientific rationale for such effect of ions on volume regulation in this letter, based on impetuous opinion, but to further our work will definitely unfold the mechanisms from physiology of cell volume regulation to the pathophysiology behind diabetes and such disease states.

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