



SDI FINAL EVALUATION FORM 1.1

PART 1:

Journal Name:	International Journal of Biochemistry Research & Review
Manuscript Number:	Ms_IJBCRR_24489
Title of the Manuscript:	Disruption of disulfide bonds of insulin receptor as a cause of insulin resistance
Type of Article	Commentaries and Opinions

PART 2:

FINAL EVALUATOR'S comments on revised paper (if any)	Authors' response to final evaluator's comments
This "Commentaries and Opinions" manuscript has serious problems. As the author(s) states in the Introduction "While resistance observed is to endogenous insulin, the exogenously administered insulin is still effective". If this statement is correct, the insulin receptor itself is normal in DM2 as oppose to the author(s)' opinions that the insulin receptor lacks disulphide bridges. Although the author(s) mentions that insulin binds to only alpha chains, it has been demonstrated that insulin binds to both of alpha- and beta-chains of the insulin receptor. The author(s) only cites very old papers in the 70's and 80's to explain mechanisms underlying activation of the insulin receptor. The references must be updated. There are uncountable numbers of typos.	1) Administered insulin is still effective in cases of DM2, as is seen in day to day practice. This is evidenced by the control of hyperglycaemia in DM2 patients on institution of insulin therapy. This is where, insulin secreted by the pancreas fails in cases of DM2, in spite of hyperinsulinemia , as evidenced by the uncontrolled hyperglycaemia. The effectiveness of administered insulin would not have been possible , if the same metabolic condition Prevailed, as in the case of untreated cases of DM2 in whom insulin was not administered. Insulin resistance is accepted to result when energy metabolism shifts from one based on carbohydrates(physiological) to one based on b oxidation of fats(pathological, as in DM2). The clinical effectiveness of insulin therapy and consequent control of hyperglycemia suggests the reversal of beta oxidation At the same time the disulfide bond formation , disrupted during the prevailing beta oxidation condition (ie untreated DM2) is resumed when carbohydrate metabolism is re-established . So clearly according to the hypothesis, the state of disulfide bonds is not the same before and after the administered exogenous insulin. Hence, the contention of the reviewer is erroneous and borne out of improper understanding of the proposed hypothesis. The exact mechanism of how this shift of metabolism on administration of insulin occurs has not yet been deciphered. No attempt is made to hazard a guess in this matter by this hypothesis. This hypothesis is a small step in the direction as to how exogenously administered insulin is effective in DM2. 2) The receptor-binding site for insulin is C- terminal of alfa sub unit of the IR. The reviewer is requested to verify his contention. 3) The suggestion about the references is noted. The hypothesis is a bridge between the facts known for decades but which were failed to be correlated in light of developments in other fields of medicine. 4) Typos were taken care of. 5) The author thanks the reviewer for his valuable suggestions for the improvement of the article.