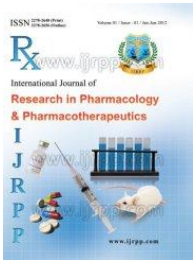
International Journal of Research in Pharmacology & Pharmacotherapeutics



ISSN Print: 2278-2648 ***IJRPP |Vol.5 | Issue 3 | July - Sep - 2016***
ISSN Online: 2278-2656 ***Journal Home page: www.ijrpp.com***

Research article ***Open Access***

Prediction of target enzyme for diabetes mellitus by isolated blood samples

G. Nagaraja Perumal* and S.Mohan

[1]*Faculty of Pharmacy, Shri Jagdishprasad Jhabarmal Tibrewala University, Jhunjhunu-333001.*
[2]*Rajasthan, India & Karpagam College of Pharmacy, Coimbatore-641032, Tamil Nadu, India.*
***Corresponding author: G. Nagaraja Perumal**

ABSTRACT

Diabetes Mellitus is a serious problem universally, by and large in both developing as well as underdeveloped nations. Conversely, a synthetic drug management of diabetes mellitus creates an unexpected adverse effect towards all organs and it is not safeguarding too. However, numerous enzymes, which is a real concern and may be accountable for diabetes mellitus and its associated complications, which would certainly afford a plenty of scope and platform to explore out the main target enzyme. These enzymes are to be targeted in treating diabetes mellitus may have a proven advantage in reducing the diabetes mellitus consequences. There are several evidences indicated Protein Tyrosine Phosphatase and variety of isomers are responsible diabetes mellitus, however Protein Tyrosine Phosphatase and its isomers are hardly targeted, due to inappropriate clinically validation lapse. Researchers are clinically validating the indeterminate Protein Tyrosine Phosphatase to establish an efficient method for variability of Protein Tyrosine Phosphatase enzyme levels of various clinical conditions of diabetes mellitus and its associated diseases.

Keywords: Diabetes Mellitus, Protein Tyrosine Phosphatase Synthetic drugs, clinically validation and Researcher.

INTRODUCTION

Diabetes mellitus has aggravated prevalence in the human population due to autoimmune obliteration of the β-cells of the pancreas through resulting insulin paucity [1-7]. The World Health Organization (WHO) predictable throughout status to diabetes mellitus and exist 7th foremost motive of casualty in 2030 and also addition it force double flanked by 2005 plus 2030 [8-11]. Present is a immense need for unambiguous enzyme target of precise metabolic complications for diabetes mellitus. Protein Tyrosine Phosphatase receptor is single central opening for triggering the insulin receptors to liberate the vital capacity of insulin. Protein Tyrosine Phosphatase receptors and its subtypes (PTP1A, PTP1B, PTP1C, PTPN1, PTPN20CP, PTPN3, PTPN4, PTPN5, PTPN6, PTPN7,PTPN9, PTPN11, PTPN12, PTPN13, PTPN14, PTPN18 PTPN20, PTPN21, PTPN22 &PTPN23) offered, which is responsible for diabetes mellitus but its clinical value is mysterious [12-19]. The curative plants and synthetic anti diabetic medicines approaches towards healing of diabetes mellitus but doesn't know the exact intention enzyme for type II diabetes mellitus [12, 42 & 21-23]. Based on the above reasons,

systematic justification is obligatory Protein Tyrosine Phosphatase receptors and its sub types.

The hypothesis

The hypotheses are proposed to find the target enzyme and its subtypes, by may be collection of blood sample from diabetic patients.

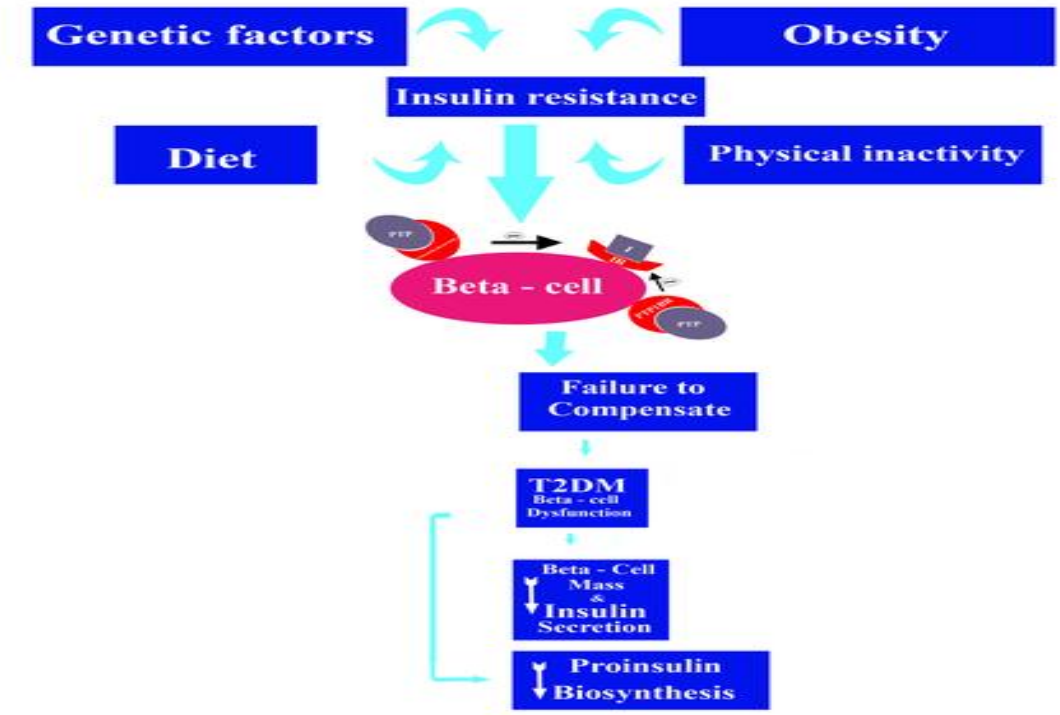


Fig:1 (Abbreviations: IR-Insulin Receptor, I-Insulin, PTP- Protein Tyrosine Phosphatase) Has indicated Protein Tyrosine Phosphatase 1B (PTP1B) is a molecule that negatively regulates Insulin Receptor. In addition to insulin sensitization, inhibition of PTP1B has potential to promote weight loss, which is a benefit since obesity largely contributes to the type 2 DM pathology.

Evaluation of the hypothesis

Although Protein Tyrosine Phosphatase and subtypes (Fig-I) for their working mechanism against diabetes mellitus and associated diseases have not been well understood, the two main afferent input to trigger insulin receptor to regulate the insulin release from beta cell and activation of glucose transporters. Other category of causative factors like PPR Gama, DDP-4, glycolysis and gluconeogenisis are clinically validated but more number of drugs promoted, which can't completely cure the diabetes mellitus [24-26]. Research suggestion shall be ready and set onward some Hospital have Institutional Ethical Committee. Consequent to the Institutional Ethical Committee ahead approval for research work shall be initiated. Characteristic guiding principle based, feedback form might be primed and a consent from diabetologist in the direction of the collection of tolerant data and Pharmaceutical care issues. The variety which control demographic data like age, sex, social history, family history, current treatment regimen, change of prescription drugs and current position of blood glucose level. In my limitation has expressed background for applying different inputs of subsequent two criteria must be measured such as 1. Inclusion criteria: a. Patient age, b. Patient with diabetes mellitus and with extra Co-morbidities, c. Patient diabetes mellitusitted as In-patient. d. Patient effortlessly to read and write the consent form and 2. Exclusion criteria: a. Patient age, b. Patient visited diabetology department without diabetes mellitus, c. Patient attenders and bystanders and d. Patient who

unable to read and write the consent form [27-45]. Based on the criteria mentioned above, specified number of patients selected for scrutiny, hence segregated different groups such as Type-I, Type-II and associated diseases with Type-I & II for collect the blood samples, which subjected to Protein Tyrosine Phosphatase analysis.

Protein Tyrosine Phosphatase Estimation

The T-Cell Flourimetric Assay Kit will be purchased abnova, sigma Aldrich, which will used to estimate the amount of Protein Tyrosine Phosphatase levels in DM and associated diseases conditions and also available two methods such as one step process and two-step process. First 10+10 sample were performed one step + two step methods for the purpose to select the method of PTP analysis, which was economically and also get accurate result.

RESULTS AND DISCUSSION

Prophylaxis strategies for management of diabetes mellitus are mainly based on patents risk. The Protein Tyrosine Phosphatase and its subtypes most widely used as risk assessment tool for risk stratification in diabetes mellitus [28-29]. However sensitivity and specificity of (Table –I), Shown Protein Tyrosine Phosphatase for an hodgepodge of clinical conditions of Type-II diabetes mellitus placid augmented in the human body when compared to apiece supplementary allied diseases and additional parameters resembling different types of receptors, which have type of chromosomes and mechanism of action included [52-53]. Above table will help to evaluate the performance of a customized Protein Tyrosine Phospatase 1/2 and other isomers panel for Diabetes Mellitus -risk assessment with patients [54-55]. The review scrutiny of diabetes mellitus and coupled diseases epidemiological and intention ruling studies in Tamil Nadu, will be established to the occurrence is rising exponentially in our kingdom. Our studies will be confirmed increasing diabetes mellitus and associated level were driving this epidemic. There is a vital necessity to widen appropriate strategies for avoidance of diabetes mellitus and associated disease in India by population based approaches, which may valuable to discover the interaction sandwiched between PTP isomers and its antagonist drugs. This hypothesis will be useful for diabetes mellitus research workers to discover new enzymes, and its subtype for the management of diabetes mellitus by the help of some micro oraganisms [56-60] and to further diminish the occurrence of diabetes mellitus associated risks.

Table- I, Multiple-enzyme sequencing sheet indicated Protein Tyrosine Phosphatase disturbed various detached situation

Sl. No	Clinical Condition	Receptors	Chromosomes	Mechanism	PTP Level in Blood	References
1	Normal	PTP and all isomers	12q15-q20	Trigger Insulin Receptor	20-30 µg/100ml	[29]
2	Type-1DM	PTP1A,B,C,N22	20p13,12q15-q21,1q-31-q32 & 2q-35-q36.1	β_2 integrin adhesion site action	Mild increased	[54&30]
3	Type-2 DM	PTP1B,O,N22	12q15-21,2p12p13-p12 & 2q-35-q36.1	RPTPα localize adhesion	Moderately increased	[54&31]
5	Type-2DM Associated Hypertension	PTP1A,D,C	12q15-q20,9p24.1-p23&1q31-q32	Focal adhesion formation	More increased	[54&33]
6	Type-2DM Associated Asthma	PTP1A,B,V	20p13,12q15-q21 & 12q15-q21	Inhibit integrin	Marked level increased	[54&35]
7	Type-2 DM Associated Cardiovascular	PTP1A,B,C,N22,U	20p13,12q15-q21,1q-31-q32, 2q-35-q36.1 & 1p35.3	Activation of mutation	Marked level increased	[54&36]

REFERENCES

[1]. Mohan S and Nandha kumar L. Role of various flavonoids: Hypotheses on novel approach to treat diabetes. *J Med Hypotheses Ideas*.6 2014, 1-6.

[2]. Ozara Tabetabaei Malazy, Bagher Larijani and et al, A Novel Management of Diabetes by means of Strong Antoxidants' Combination. *J Med Hypotheses Idea*s. 7, 2013, 25-30.

[3]. IDF diabetes atlas. *International Diabetes federation*.15, 2011, 1-120.

[4]. Abdollahi M, Ranjbar A and Shadnia. Pesticides and oxidative stress: A review. *Med Sci Monit*.10, 2004, 141–147.
[5]. Rahimi R, Nikfar S and Larijani B. A review on the role of antioxidants in the management of diabetes and its complications (Carolina USA). *Biomed Pharmacother*. 59, 2005, 365–73.
[6]. Guyton A C and Hall J E, Text Book of Medical Physiology. New York, McGraw Hill; United States of America. 1996, 855-863.
[7]. Stphen G N Davis and Daryl K Granner, the Pharmacological Basis of Therapeutics. Edn 5 Vol 1 Pharmacology of the Endocrine Pharmacology, McGraw Hill Professional, New York, USA, 2010, pp.1679-1715.
[8]. Global health risks, Mortality and burden of disease attributable to selected major risks. *World Health Organization*, 2009, 1-127.
[9]. Danaei G, Finucane MM, Lu Y, Singh GM, National, regional and global trends in fasting plasma glucose and diabetes prevalence since 1980: Systematic analysis of health examination surveys and epidemiological studies with 370 country-years and 2.7millionparticipants. *Lancet*. 378 2011. 31–40.
[10]. Mathers CD and Loncar D, 2006. Projections of global mortality and burden of disease from, to 2030. *PLoSMed*, 3, 2002, 442.
[11]. Harris M Alberti K,Zimmet P, Defronzo R. And Zimmet P. International Text Book of Diabetes Mellitus. Edn 7 Vol1 Chichester, John Wiley and Sons publication United Kingdom, 1997, 9–23.
[12]. Ta.batabaei-Malazy O, Larijani B and Abdollahi M. A systematic review of in vitro Studies conducted on effect of herbal products on secretion of insulin from Langerhans Islets. *J Pharm Sci*. 15, 2012,447–466.
[13]. Mohammadi M, Atashpour S and Pourkhalili. Comparative improvement in function of isolated rat Langerhans islets by various phosphodiesterase 3, 4 and 5 inhibitors. *Asian J Anim Vet Adv.*12, 2011, 233–40.
[14]. Mehri A, Hasani-Ranjbar S and Larijani B, A systematic review of efficacy and safety of Urtica dioica in the treatment of diabetes. *Int J Pharmacol*. 7, 2011, 161–70.
[15]. Mohseni-Salehi-Monfared SS and Larijani B. Islet transplantation and antioxidant management: a comprehensive review.*World J Gastroenterol*. 15, 2009, 1153–61.
[16]. Matthias M. Ledig, Fawaz Haj and [John] L. Bixby. The Receptor Tyrosine Phosphatase Crypα Promotes Intraretinal Axon Growth. *J.Cell Biol.* 18, 1999, 375– 388.
[17]. Angiola Petrone and Jan Sap. Emerging issues in receptor protein tyrosine phosphatase function: lifting for simply shifting?. *J Cell Scie*. 113, 2000, 2345- 2354.
[18]. Jeffrey D Bjorge, Andrew Jakymiw and Donald J Fujita. Selected glimpses into the activation and function of Src kinase. *Oncogene*. 21, 2000, 5620-5635.
[19]. Sundaram Nambirajan, Vegesna Radha and Shubhangi Kamatkar. PTP-S2, a nuclear tyrosine phosphatase, is phosphorylated and excludedfrom condensed chromosomes during mitosis. *J Biosci*.25, 2000, 33-40.
[20]. Barbara Tremper-Well, Ross J. Resnick1in Zheng and Leslie J. Holsinger2.Extracellular domain dependence of PTP A transforming activity Shalloway. *Genes to Cells*.15, 2010, 711–724.
[21]. Tzu-Ching Meng and Toshiyuki Fukada Reversible Oxidation and Inactivation of Protein Tyrosine Phosphatases *InVivo*. *Mol Cell*.9, 2002, 387–399.
[22]. Kjeld Norris' Fanny Norris, Dwight H Kono and Henrik Vestergaard. Expression of Protein-tyrosine phosphatases in the major insulin target tissues. *FEBS Letters*, 415 1997, 243-24.
[23]. John V. Frangioni, Pamela H. Beahm and Victor Shifrin. The nontransmembrane tyrosine phosphatase PTP-1B localizes to the endoplasmic reticulum via its 35 amino acid C-terminal sequence *Cell*. 68, 1992, 545-560
[24]. Zhang Z.Y and Dixon J.E. Active site labeling of the Yersinia Protein Tyrosine Phosphatase: the determination of the pKa of the active site cysteine and the function of The conserved histidine 402 . *Biochem*.32, 1993, 9340–9345.
[25]. Wiljan J.A.J. Hendriks and Rafael Pulido. Protein tyrosine phosphatase variants in human hereditary disorders and disease susceptibilities. *Biochimica et Biophysica Acta*.10, 2013, 1673-1696.
[26]. Thareja S, Aggarwal S and Bhardwaj; Protein tyrosine phosphatase 1B inhibitors: a molecular level legitimate approach for the management of diabetes mellitus. *Med Res Rev.* 32, 2012, 459-517.

[27]. Rong-jun He, Zhi-hong Yu and Ruo-yu Zhang. Protein tyrosine Phosphatases as potential therapeutic targets. *Acta Pharmacol Sin,35*, 2014,1227– 1246.

[28]. Yang Y, Gil MC and Choi EY. Molecular cloning and chromosomal localization of a human gene homologous to the murine R-PTP-kappa, a receptor-type protein tyrosine phosphatase. *Gene*, 20, 1999, 77-82.

[29]. Faiyaz Ahmad, John L. Azevedo, Jr and Ronald Cortright. Goldstein Alterations in Skeletal Muscle Protein–Tyrosine Phosphatase Activity and Expression in Insulin-resistant Human Obesity and Diabetes. *J. Clin Invest.100*, 1997, 449–458.

[30]. Jeffrey D. Bjorge, Andrew Pang and Donald J. Fujita, Identification of Protein-tyrosine Phosphatase 1B as the Major Tyrosine Phosphatase Activity Capable of Dephosphorylating and Activating c-Src in Several Human Breast Cancer Cell Lines. *The J Biol Chem.275, 2000*, 41439-41446.

[31]. Angeliki Malliri and John G Collard, Role of Rho-family proteins in cell adhesion and Cancer. *Curr Opin Cell Biol*.15, 2003, 583-589

[32]. Sheila M. Thomas and Joan S. Brugge Cellular Functions Regulated By Src Family Kinases. *Annu Rev Biol*. 13, 1997, 513-609.

[33]. Yoshimasa Nakamura, Nikolay Patrushev and Hyoe Inomata. Role of Protein Tyrosine Phosphatase 1B in Vascular Endothelial Growth Factor Signaling and Cell–Cell Adhesions in Endothelial Cells. *Cir Res.102*, 2008, 1182-1191.

[34]. Yang Y, Gil MC and Choi EY. Molecular cloning and Chromosomal localization of a human gene homologous to the murine R-PTP-kappa, a receptor-type protein tyrosine phosphatase. *Gene*.186, 1997, 77-82.

[35]. Jamieson CR, van der Burgt I and Brady AF. Mapping a gene for Noonan syndrome to the long arm of chromosome 12. *Nat. Genet*. 8, 1994, 357-360.

[36]. Freeman RM Jr, Plutzky Jand Neel BG.Freeman. Identification of a human src homology 2-containing protein-tyrosine-phosphatase: A putative homolog of Drosophila. *Natl. Acad. Sci*. 23, 1992, 11239-11243.

[37]. Roach T, Slater S and Koval M, CD45 regulates src family member kinase activity associated with macrophage integrin- mediated adhesion. *Curr Biol*. 7, 1997, 408–417.

[38]. Eok-Soo Oh, Haihua Gu, Tracy M and et al, Regulation of Early Events in Integrin Signaling by Protein Tyrosine PhosphataseSHP-2. *Mol Cell Biol*. 19, 1999, 3205– 3215.

[39]. Global status report on noncommunicable diseases. *World Health Organization*. 2010, 101- 110.

[40]. Quang Nguyen, Loida Nguyen and James V Felcetta, Evaluation and Management of Diabetes Mellitus. *America.Heal & Drug Benefits*. 1, 2008, 1-8.

[41]. Pranav K. Prabhakar and Mukesh Doble. A Target Based Therapeutic Approach Towards Diabetes Mellitus Using Medicinal Plants. *Current Diabetes Review. 4*, 2008, 291-308.

[42]. Abiru N, Takino H and Yano M. Clinical Evaluation of Non-Insulin Dependent Diabetes Mellitus Patients with Auto Antibodies to Glutamic Acid Decarboxylase. *J.Autoimmun*. 5, 1996, 683-688.

[43]. James R. Sover and murray Epstein. Diabetes Mellitus Associated Hypertension, Vascular Disease and Nephropathy Cells. *Hypertension.* 26, 1995, 869-879.

[44]. Srinivasan R and Ramya G, Adverse Drug Reaction- Causality Assessment **(**Publishers, In- IJPCR, 35, PrintersNagarII, SitabariTonkRoad, Jaipur, Rajasthan, **India).** *Int. J. Pharma.Clinical*.13, 2011, 2231-34.

[45]. Dabhade suhas and Bhosle Dr.Deepak, Review on Pharmacovigilance study of Telmisartan in Hypertension Patients. *Asian.J.Pharma.Clinic.Res.*6, 2013, 10974- 75.

[46]. James M:Mc Kenney, Judith M. Slining and Richard Henderson. The Effect of Clinical Pharmacy Services on Patients with Essential Hypertension. *Cir*. 48, 1973, 1104-1111.

[47]. Mandavi, Sanjay D Cruz, Atul Sachdev and Pramil Tiwari. Adverse drug reactions & their risk factors among Indian ambulatory elderly patients. *Ind J Med Res*.136, 2012, 404- 410.

[48]. Himanshu Sharma, Mohammed Aqil, Faisal Imam. A Pharmacovigilance study in the department of medicine of a university teaching hospital. *Pharm Pract*.5, 2012, 46-49.

[49]. Law MR, Wald NJ and Morris JK. Value of Low dose Combination treatment with blood pressure lowering drugs. *Anal.BMJ*.326, 2003, 1427-31.

[50]. Adigun AQ, Ishola DA, Akintomide AO. Shifting trends in the Pharmacologic treatment of hypertension in a Nigerian tertiary hospital: a real-world evaluation of the efficacy, safety, rationality and pharmacoeconomics of old and newer antihypertensive drugs. *J. Hum. Hyp*.17, 2003, 277-285.

[51]. G.Liamis, H. Milionis and M.Elisaf. Blood pressure drug therapy and electrolyte Disturbances. *Int J.Clin Practice*.1 2008, 1572-1579.

[52]. Nilima A.Kshirsagar and Sunil Karande. Adverse Drug Reaction Monitoring in Pediatric Practice. *J. of Ind. Pediatric*.33, 1996, 993-996.

[53]. Hasford J, Mimran A and Simons WR. A Population-based European cohort study of Persistence in newly diagnosed hypertensive patients. *J. Hum. Hyp*.16, 2002, 569-575.

[54]. *Gene Nomenclature Committee* reported on Protein tyrosine phosphataseses, including dual specificity of phosphatases; 2014; *http/www.genenames.org/genefamilies/PTP*

[55]. Wright JE, Wright AM. *Bol Soc Argent Bot*. 40, 2005, 1–2.

[56]. Canas AI, Camarero S. Laccases and their natural mediators:biotechnological tools for sustainable eco-friendly processes. *Biotechnol Adv*. 28, 2010,694–705.

[57]. Lundell TK, Mäkelä MR, Hildén K. Lignin-modifying enzymesin filamentous basidiomycetes ecological, functional andphylogenetic review. *J Basic Microbiol*.5, 2010, 5–20.

[58]. Welti S, Moreau PA, and Favel A, Molecular phylogeny of*Trametes* and related genera, and description of a new genus Leiotrametes. *Fungal Div*.55, 2012, 47–64.

[59]. Baldrian P, Gabriel J. Lignocellulose degradation by *Pleurotusostreatus* in the presence of cadmium. *J FEMS Microbiol Lett*. 220, 2003, 235–240.

[60]. Preussler CA, Shimizu E, Villalba LL and Zapata PD. Review of *Trametes villosa.Rev Ciencia Tecnol*. 12, 2009, 9–16.