

**Extended duration linagliptin nanoparticles: a novel, safe and effective future of diabetes treatment?**

Muhammad Hamayal, Saira Mahmud, Warda Shahid

Dear Editor,

Diabetes Mellitus (DM), a chronic disease characterised by hyperglycaemia caused by either underproduction of insulin or defective insulin action, has become more prevalent globally; affecting 1 in every 10 adults over the past years with type 2 diabetes being more common in the low- and middle-income countries and type 1 in high-income countries<sup>1</sup>. Pakistan, being a lower-middle-income country, has a 26.7% prevalence of diabetes and age-adjusted comparative prevalence of 30.8% affecting 1 in approximately every 4th adult<sup>2</sup>. The current guidelines for the management of diabetes include insulin, metformin, sulfonylureas, and sodium-glucose co-transporters type 2 (SGLT-2) inhibitors. However, hypoglycaemia, weight gain, gastrointestinal problems and contraindication of their use in patients with pre-existing renal diseases pose problems for clinicians. Poor patient compliance in following the regular antidiabetic regimen also make treatment plans ineffective. Thus, newer drugs are constantly being researched<sup>3</sup>.

Metformin has been an excellent treatment option with only a slight risk for some specific patients to develop lactic acidosis. It is the most commonly prescribed medication for DM. Another drug, Linagliptin (Lina) was approved by the FDA in 2011 as an effective dipeptidyl peptidase inhibitor for the treatment of DM. It has been used as monotherapy and in combination with dapagliflozin, an SGLT2 inhibitor, for the treatment of diabetes in patients with a history of metformin therapy. However, its use was limited due to its low bioavailability<sup>4</sup>. Recent research suggests that the extended duration (ED) Lina via the use of poly D, L-lactic-co-glycolic acid (PLGA) polymers in nanoparticle form could be beneficial in the management of type 2 DM. It has an increased bioavailability, fewer reported side effects and a reduced

need for regular dosage. Furthermore, the use of nanoparticles facilitates a targeted delivery of the drug which may omit the pain that is caused by the use of implants<sup>5</sup>.

Lina is also thought to be effective in Type 3 Diabetes which causes Alzheimer's disease. As dementia can lead to forgetting to take medications regularly, the ED Lina, which is taken once weekly, may be a suitable option. This new formulation is being considered for its better safety profile compared to other antidiabetics and its effectiveness in controlling HbA1C both as monotherapy and in combination therapy<sup>4,6</sup>.

ED Lina in nanoparticle formulation is promptly rising as a regular guideline drug but there is an urgent need for further clinical studies and trials focusing on its specific pharmacokinetics and pharmacodynamics. Furthermore, Clinical trials to evaluate its possible side effects or adverse effects as well as its efficacy for different age groups should also be carried out.

**DOI:** <https://doi.org/10.47391/JPMA.20481>**Disclaimer:** All authors confirm that this article hasn't been published elsewhere.**Conflict of Interest:** All authors confirm that there are no conflicts of interest.**Source of Funding:** All authors confirm that there is no funding to disclose.**References**

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Final Year MBBS Student, Federal Medical College, Islamabad, Pakistan.

**Correspondence:** Muhammad Hamayal. Email: [Hamayalkhan2@gmail.com](mailto:Hamayalkhan2@gmail.com)**ORCID ID:** 0009-0005-4908-4844**Submission complete:** 26-03-2024**Review began:** 14-05-2024**Acceptance:** 01-07-2024**Review end:** 22-06-2024

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**Authors' Contribution:**

**MH:** Concept, design, literature search, data interpretation, drafting, revision and final approval.

**SM:** Concept, design, literature search, revision and final approval.

**WS:** Concept, data interpretation, drafting and final approval.