

**Structural repositioning, *in-silico* molecular modeling, oxidative degradation, and biological screening of linagliptin as adenosine 3 receptor (ADORA3) modulators targeting hepatocellular carcinoma**

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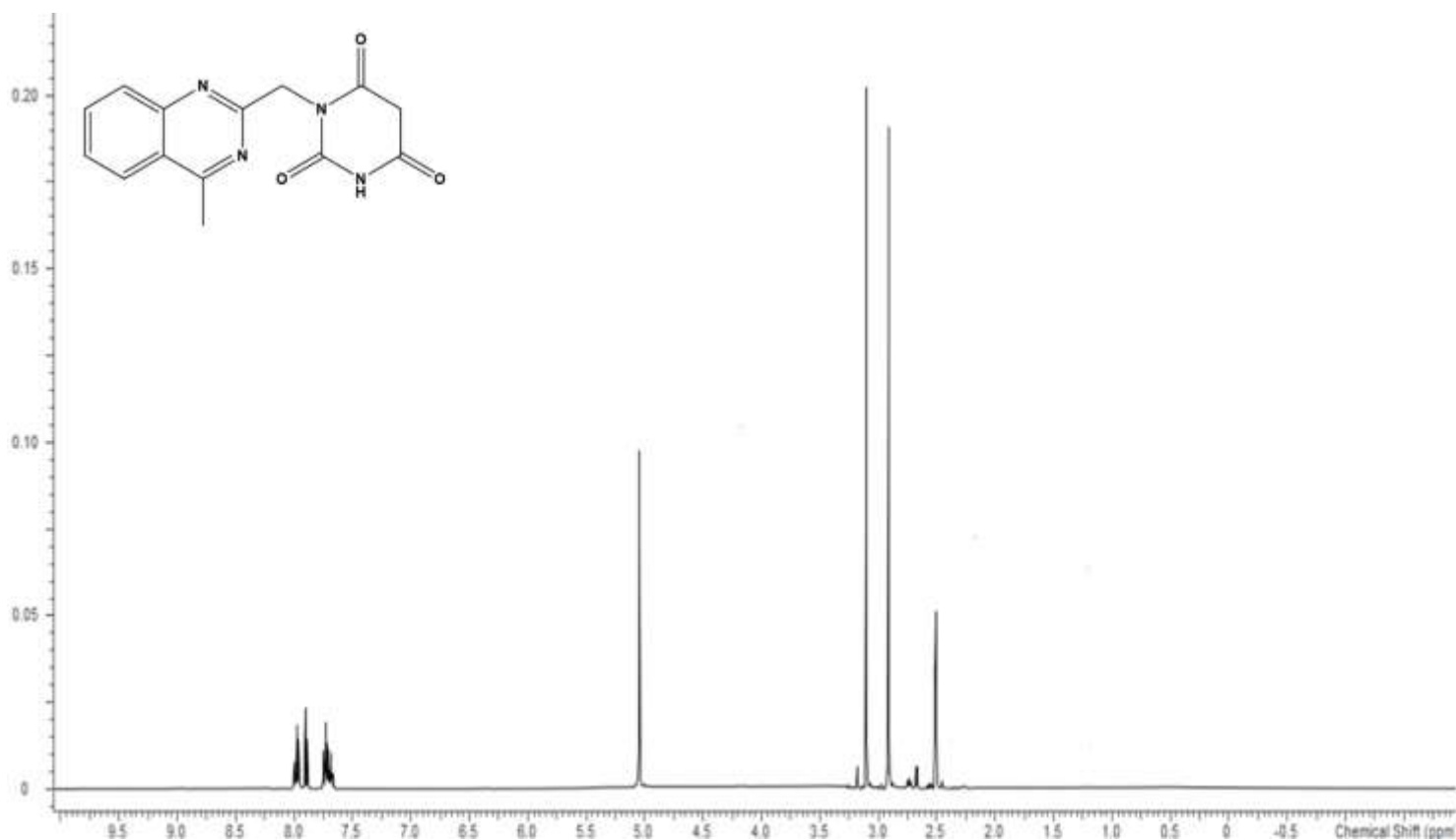
The Center for Drug Research and Development (CDRD)

Faculty of Pharmacy, The British University in Egypt

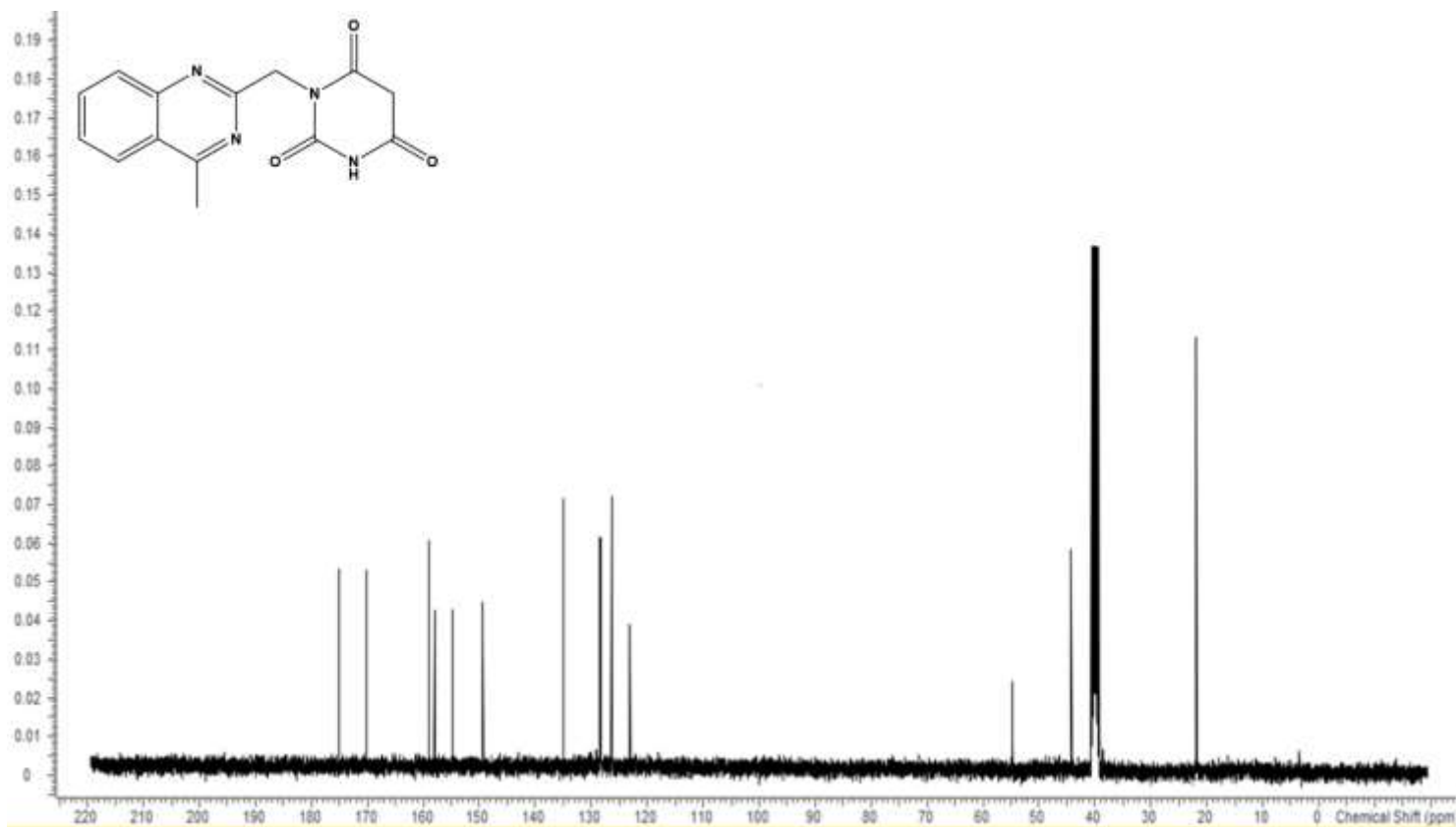
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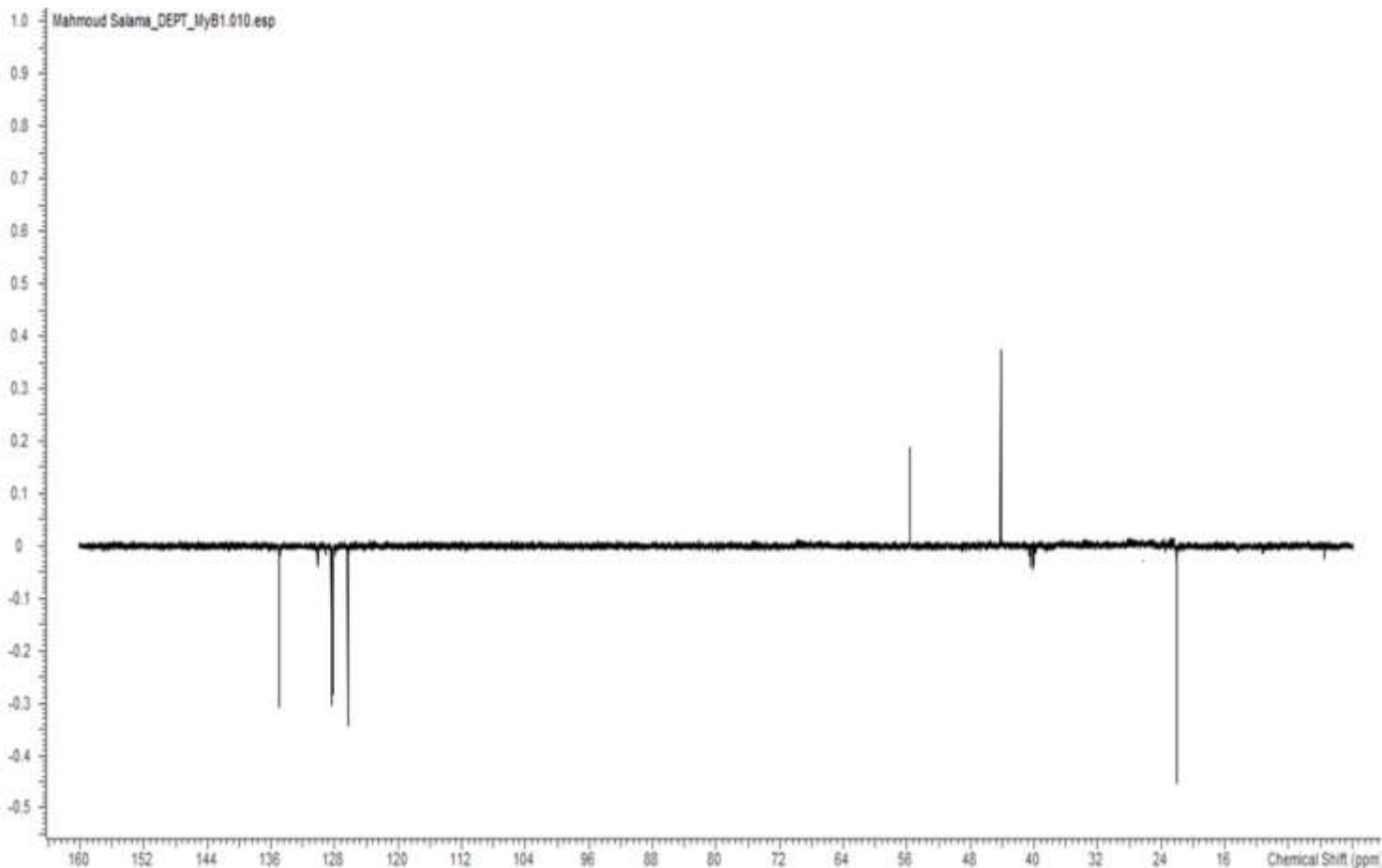
**Supporting Data**



**Figure S1:** <sup>1</sup>H NMR spectra for Degradation Product (DEG)

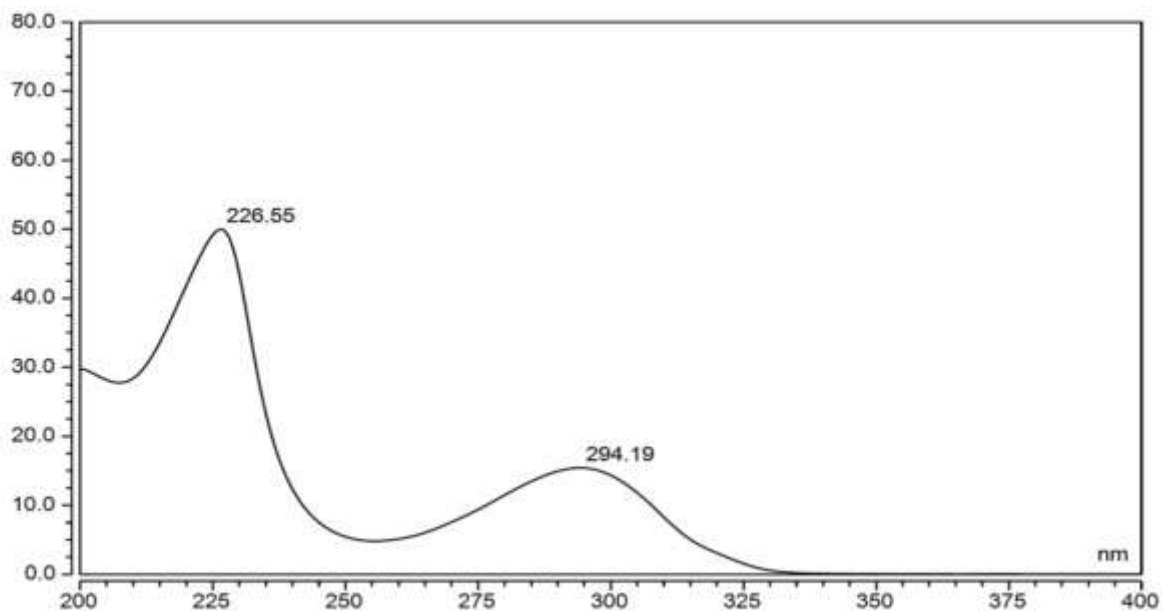


**Figure S2:**  $^{13}\text{C}$  NMR spectra for Degradation Product (DEG)

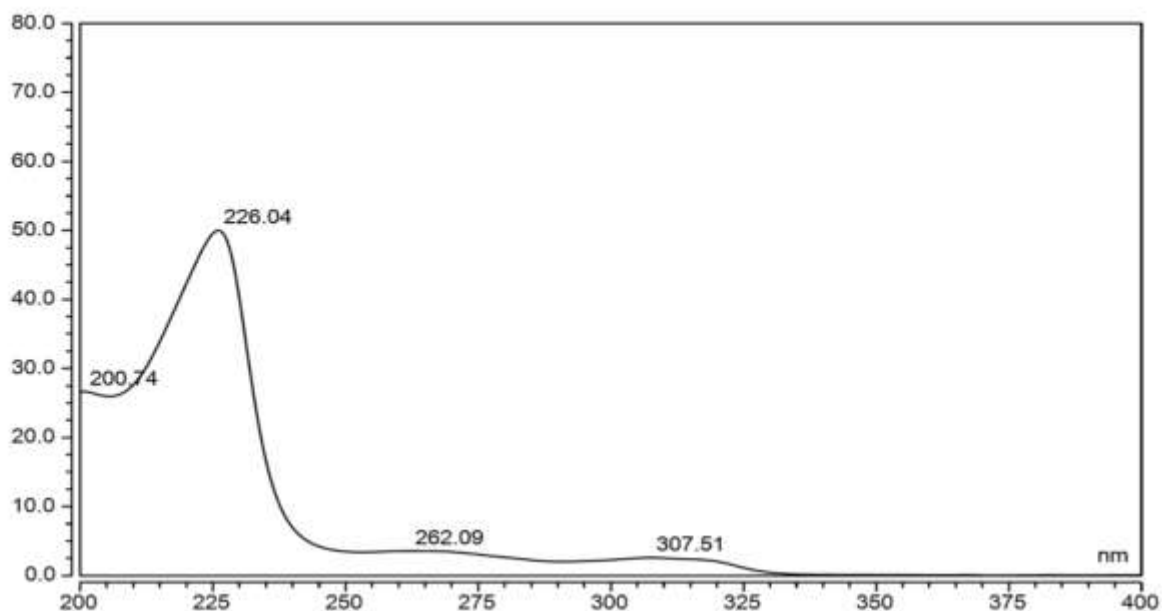


**Figure S3:** DEPT135 spectra for Degradation Product (DEG)

a)



b)



**Figure S4:** 3D spectrum scan of (a) Linagliptin and (b) the proposed degradation product.

**LC-MS/MS chromatographic and mass spectrometric conditions:**

The whole The column temperature was kept at 25°C, the injection volume used was 10 µL, and the flow rate was 0.3 mL/min with 3 min as the run time. Cone voltage was set at 30 V; source temperature was set at 150°C, and the collision energy was set at 30 eV for both drugs to enable multiple reaction monitoring (MRM) of the transition pairs

of m/z 473.11 to 420.07 for LIN and m/z 285.05 to 156.93 for DEG in the positive mode utilizing Electro Spray Ionization (ESI). The following parameters were applied: turbo ions spray at 400°C, capillary temperature at 275°C, sheath and auxiliary gas at 15 and 2 psi, respectively, ion spray voltage of 3800 V, capillary voltage of 4 KV, capillary offset of 35 and de-solvating line temperature at 400°C.