"Development of novel Thiazolidine-2,4-Dione Derivatives as PPAR-γ Agonists through Design, Synthesis, Computational Docking, MD Simulation, and Comprehensive invitro and invivo Evaluation"

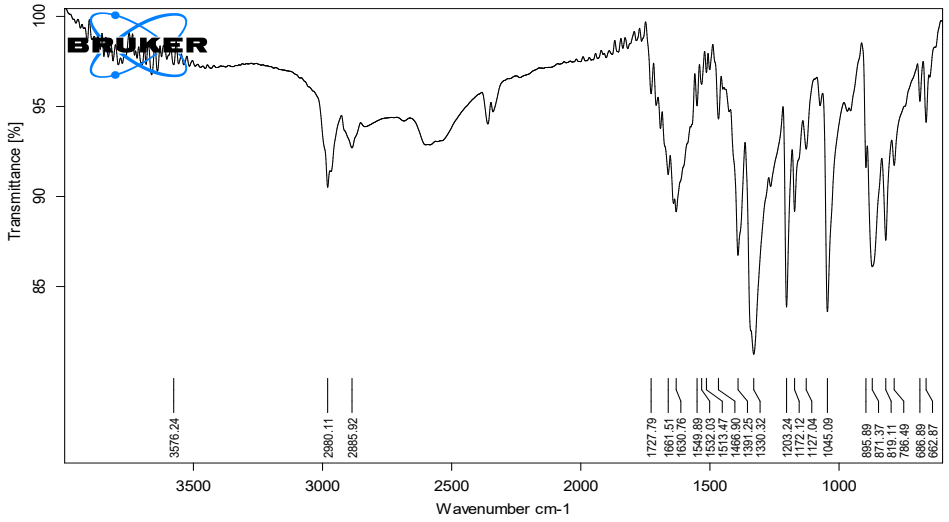
[1]Mahendra Gowdru Srinivasa, [1]Revanasiddappa B C*, [2]Ashwini Prabhu, [2]Vinitha Rani, [3]Sudeep D. Ghate, [4]Prashantha Kumar B R.

Analytical data

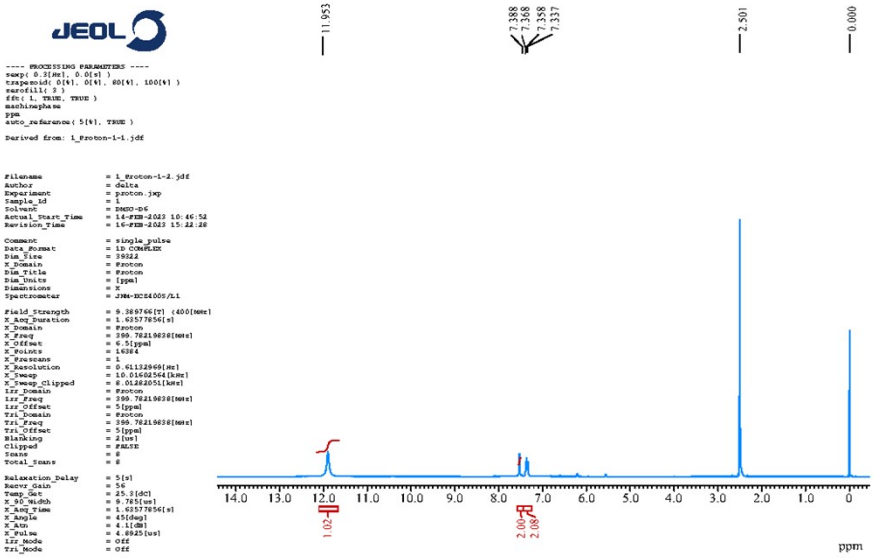
(Z)-5-(Thiophen-2-ylmethylene) thiazolidine-2,4-dione

Yellow solid, yield 80%, mp196–198 °C, FT-IR (KBr, cm−1): 3576.24 (NH), 2980.11 (C–H),1727.79 (C=O). 1H-NMR (δ ppm, DMSO-d6): 7.337-7.388 (m, 4H, Ar-H), 11.953 (s, 1H, NH). 13C-NMR (δppm, DMSO-d6): 126.110, 126.144, 127.723, 128.935, 132.085, 140.383, 154.258, and 156.774. MS (m/z): M + analyzed 210.1430, and M + predicted 210.9762.

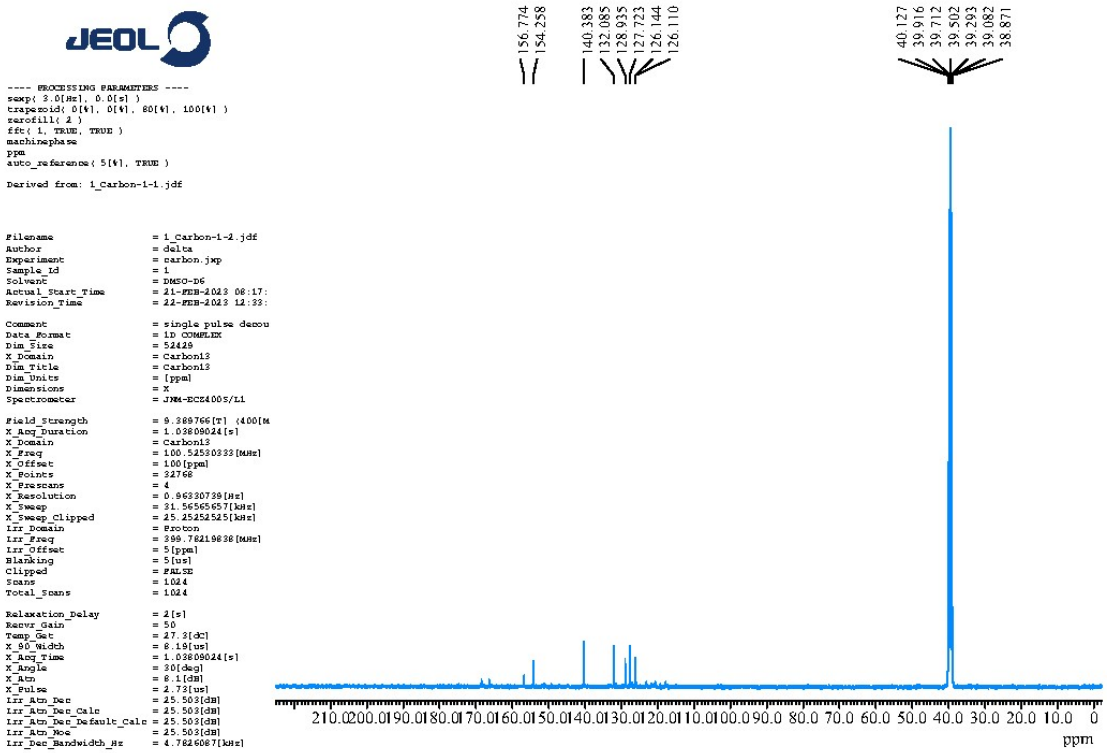
(Z)-5-(Thiophen-2-ylmethylene) thiazolidine-2,4-dione



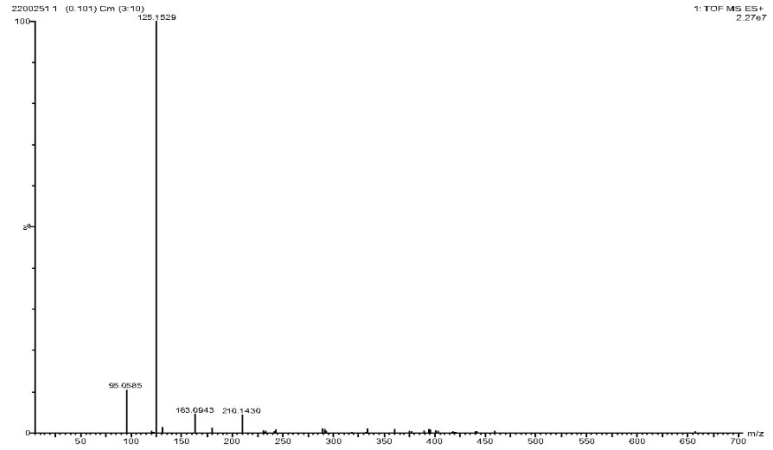
(Z)-5-(Thiophen-2-ylmethylene) thiazolidine-2,4-dione



(Z)-5-(Thiophen-2-ylmethylene) thiazolidine-2,4-dione

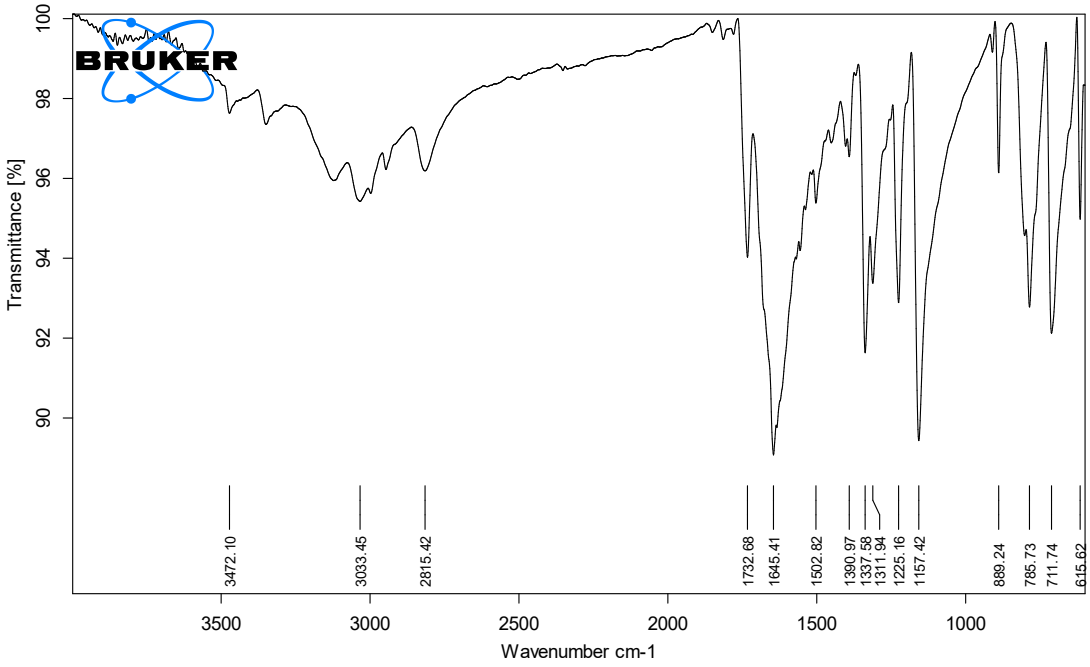


(Z)-5-(Thiophen-2-ylmethylene) thiazolidine-2,4-dione

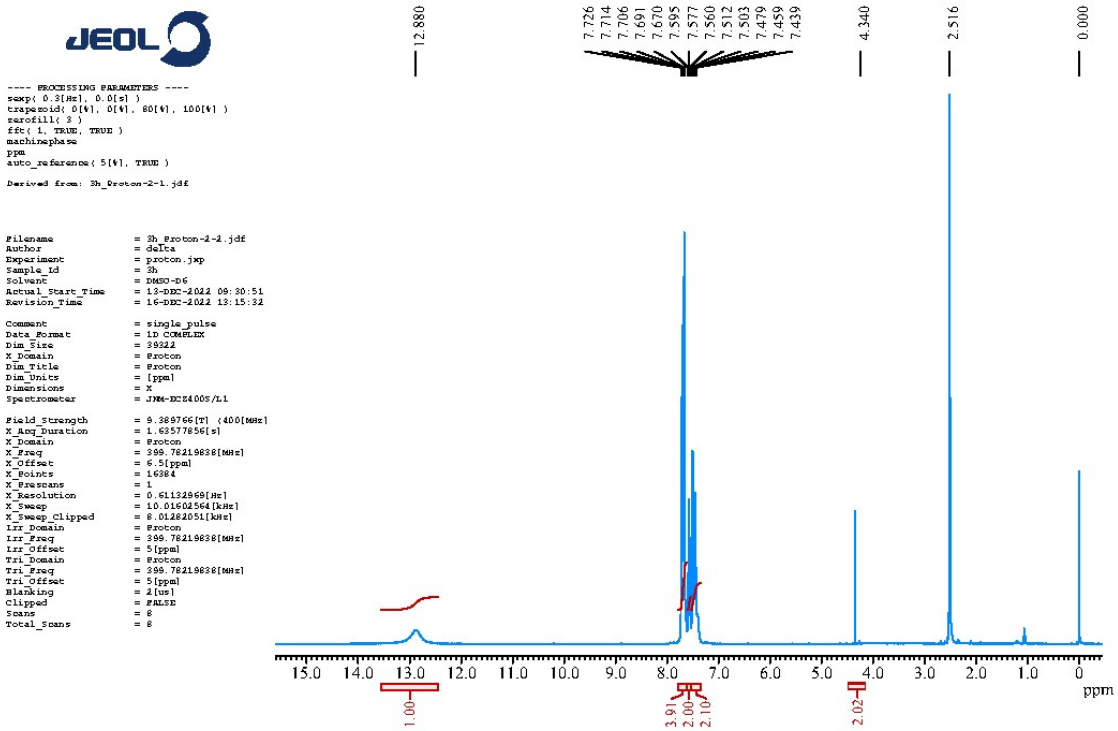


(Z)-2-(2,4-Dioxo-5-(thiophen-2-ylmethylene) thiazolidin-3-yl)-N-(3-(trifluoromethyl) phenyl) acetamide (3h): yellow solid, yield 78%, MP231–233 °C, FTIR (KBr, cm^{-1}): 3472.10 (NH),3033.45 (Ar C–H),1732.68 (C=O),1157.42 (C-N). ^{1}H-NMR (δ ppm, DMSO-*d6*): 4.340 (s, 2H, CH_2), 7.439-7.726 (m, 8H, Ar-H), 12.880 (s, 1H, NH), ^{19}F NMR (δ ppm, $CDCl_3$,): -61.412 (s, 3F, CF_3); ^{13}C-NMR (δ ppm, DMSO-*d6*): 50.17, 117.76, 120.61, 120.79, 121.55, 121.60, 123.05, 123.16, 126.10, 126.14, 127.72, 128.93, 132.08, 140.38, 154.25, 156.77, 166.32, and 168.48. MS (m/z): M+ analyzed412.0255, M+ predicted 412.4063.

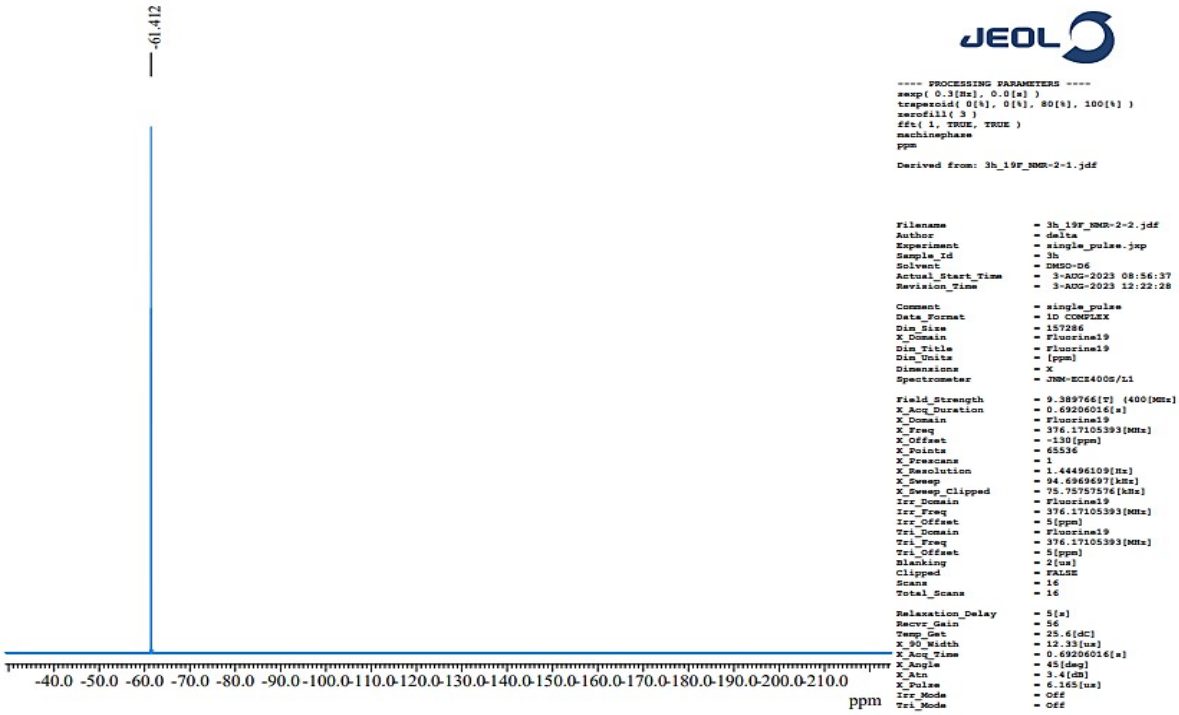
(Z)-2-(2,4-Dioxo-5-(thiophen-2-ylmethylene)thiazolidin-3-yl)-N-(3-(trifluoromethyl)phenyl)acetamide (3h)



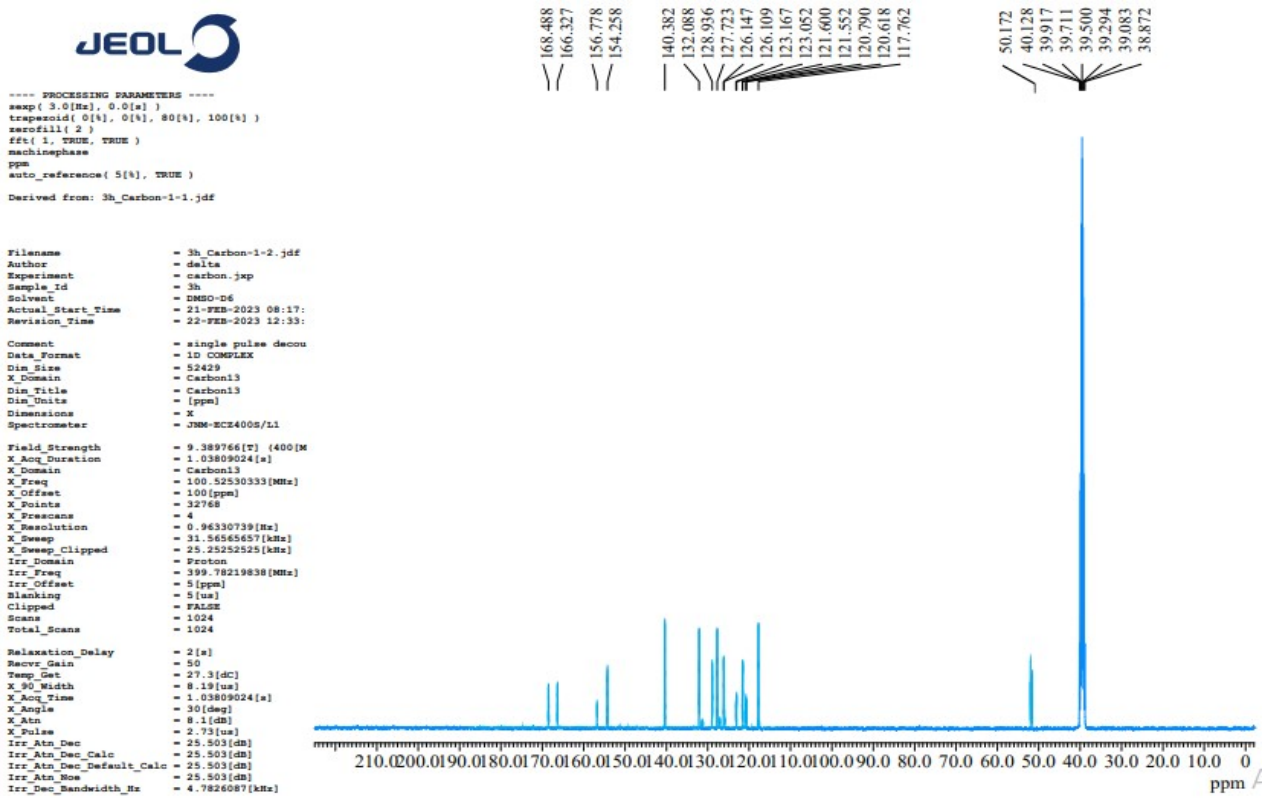
(Z)-2-(2,4-Dioxo-5-(thiophen-2-ylmethylene)thiazolidin-3-yl)-N-(3-(trifluoromethyl)phenyl)acetamide(3h):



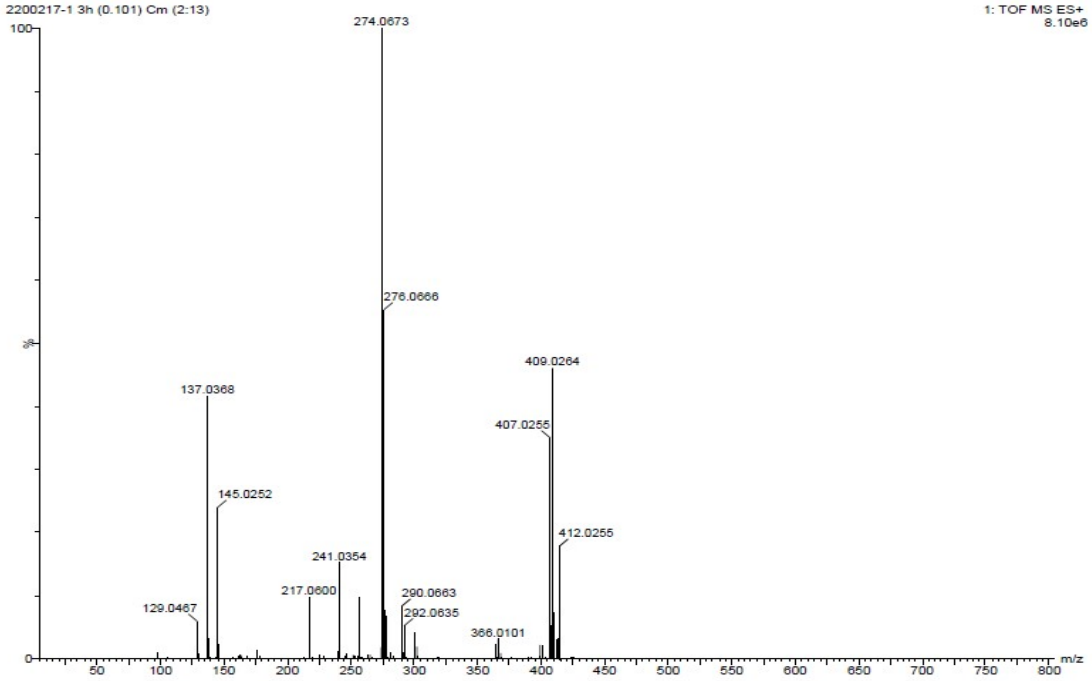
(Z)-2-(2,4-Dioxo-5-(thiophen-2-ylmethylene)thiazolidin-3-yl)-N-(3-(trifluoromethyl)phenyl)acetamide(3h):



(Z)-2-(2,4-Dioxo-5-(thiophen-2-ylmethylene)thiazolidin-3-yl)-N-(3-(trifluoromethyl)phenyl)acetamide (3h):

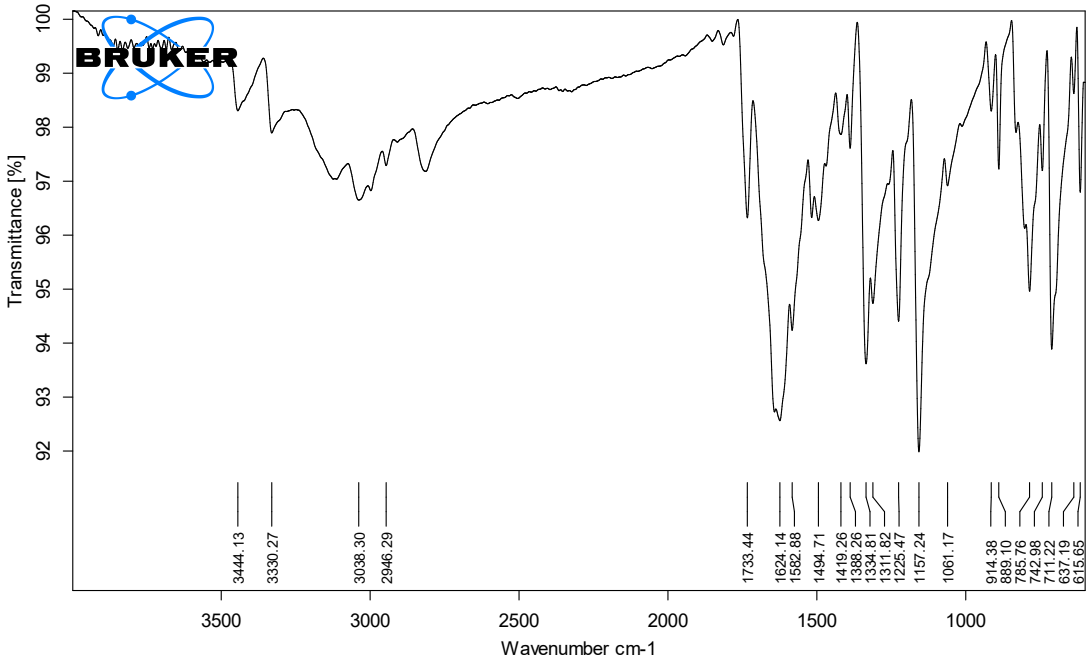


(Z)-2-(2,4-Dioxo-5-(thiophen-2-ylmethylene)thiazolidin-3-yl)-N-(3-(trifluoromethyl)phenyl)acetamide (3h):

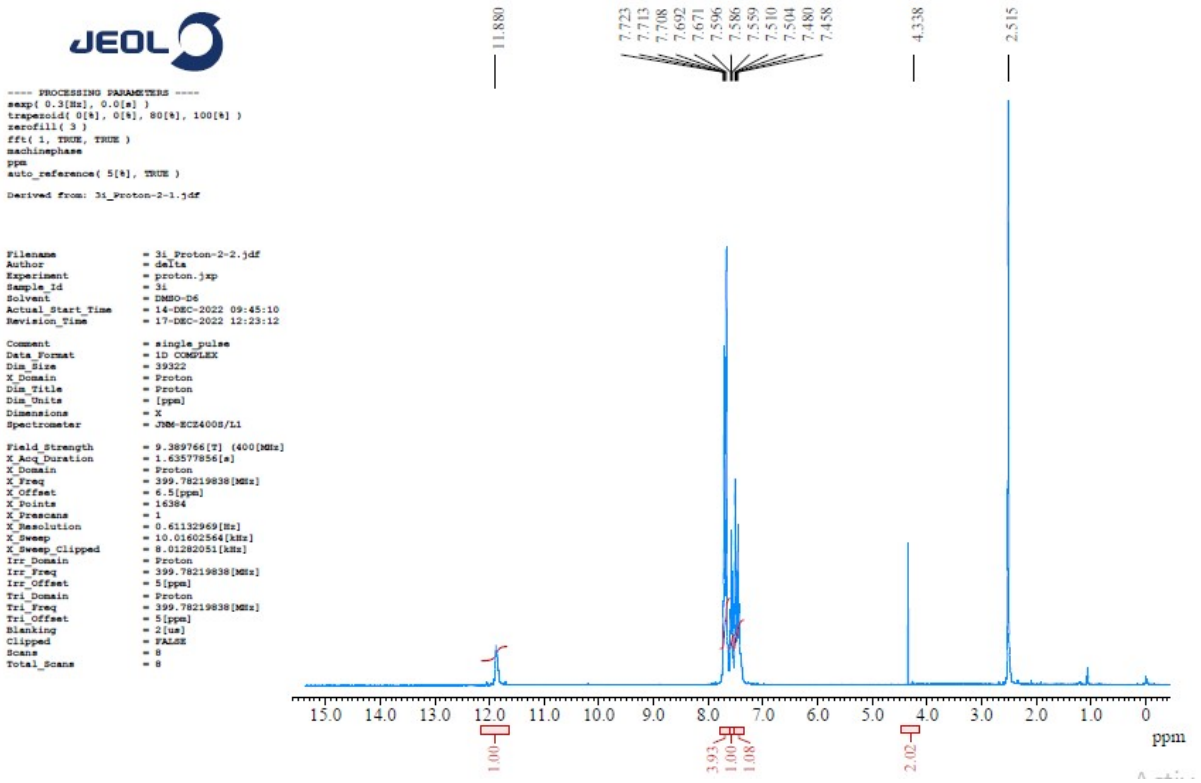


(Z)-2-(2,4-Dioxo-5-(thiophen-2-ylmethylene)thiazolidin-3-yl)-N-(2,4,5-trichlorophenyl)acetamide (3i):yellow solid, yield 81%, MP 238–240 °C, FTIR (KBr, cm^{-1}): 3444.13(NH), 3038.30 (Ar C–H), 1733.44 (C=O), 1157.24 (C-N). ^{1}H-NMR (δ ppm, DMSO-*d6*): 4.338 (s, 2H, CH_2), 7.458-7.723 (m, 6H, Ar-H), 11.880 (s, 1H, NH). ^{13}C-NMR (δ ppm, DMSO-*d6*): 51.43, 114.54, 115.86, 117.68, 118.28, 121.15, 123.59, 123.99, 127.01, 127.48, 127.65, 128.09, 129.18, 129.95, 131.25, 135.56, 145.04, and 151.85. MS (m/z): M+ analyzed 445.9410, M+ predicted 445.9120.

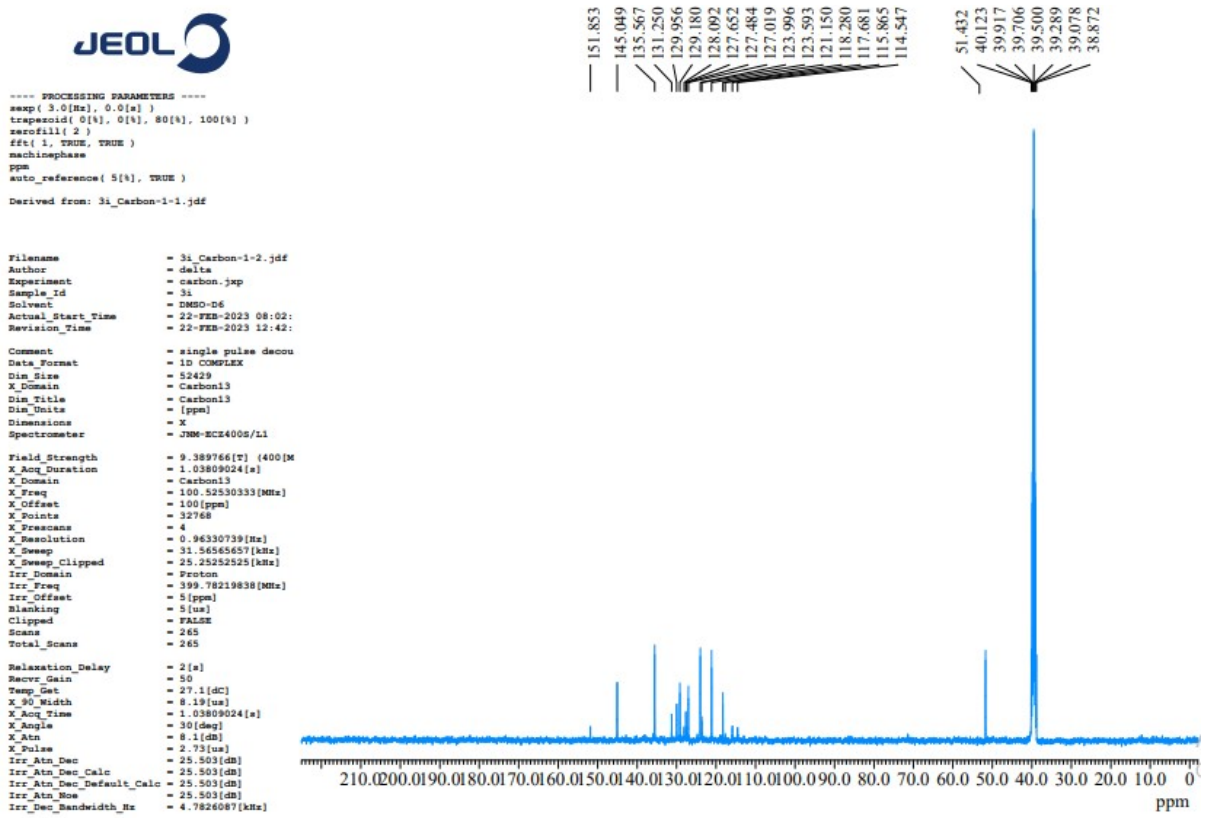
(Z)-2-(2,4-Dioxo-5-(thiophen-2-ylmethylene)thiazolidin-3-yl)-N-(2,4,5-trichlorophenyl)acetamide (3i):



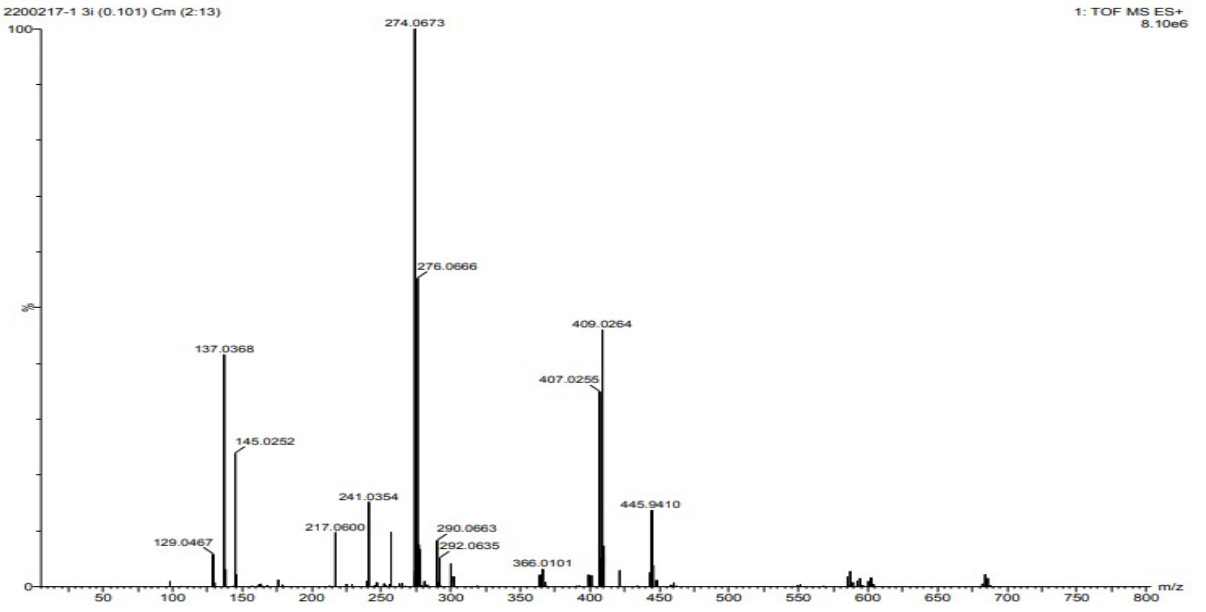
(Z)-2-(2,4-Dioxo-5-(thiophen-2-ylmethylene)thiazolidin-3-yl)-N-(2,4,5-trichlorophenyl)acetamide (3i):



(Z)-2-(2,4-Dioxo-5-(thiophen-2-ylmethylene)thiazolidin-3-yl)-N-(2,4,5-trichlorophenyl)acetamide (3i):

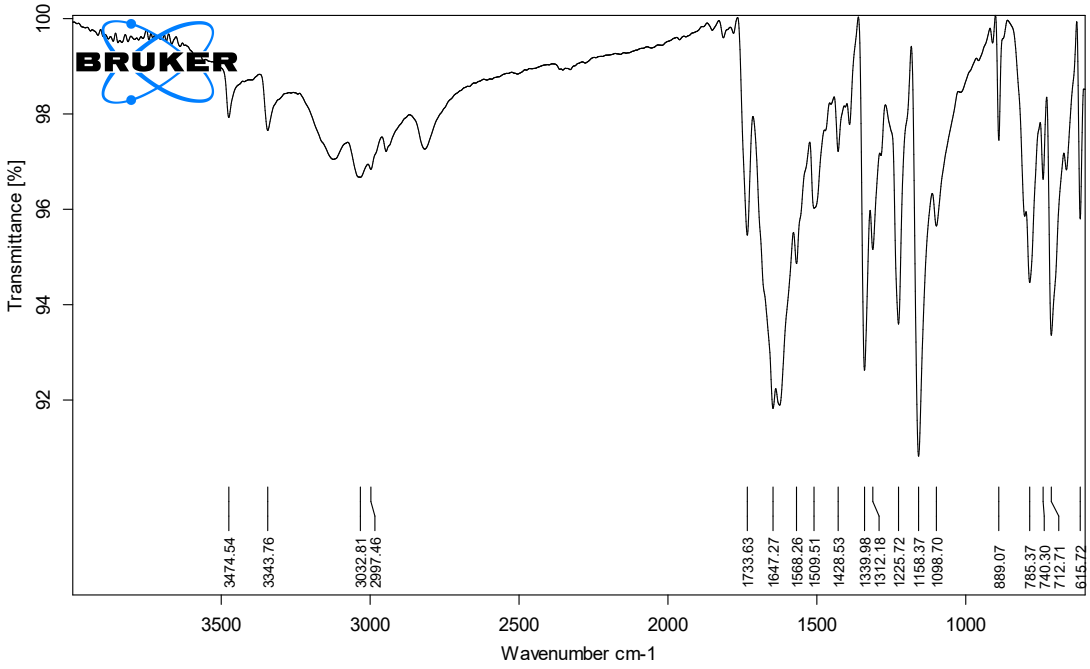


(Z)-2-(2,4-Dioxo-5-(thiophen-2-ylmethylene)thiazolidin-3-yl)-N-(2,4,5-trichlorophenyl)acetamide (3i):

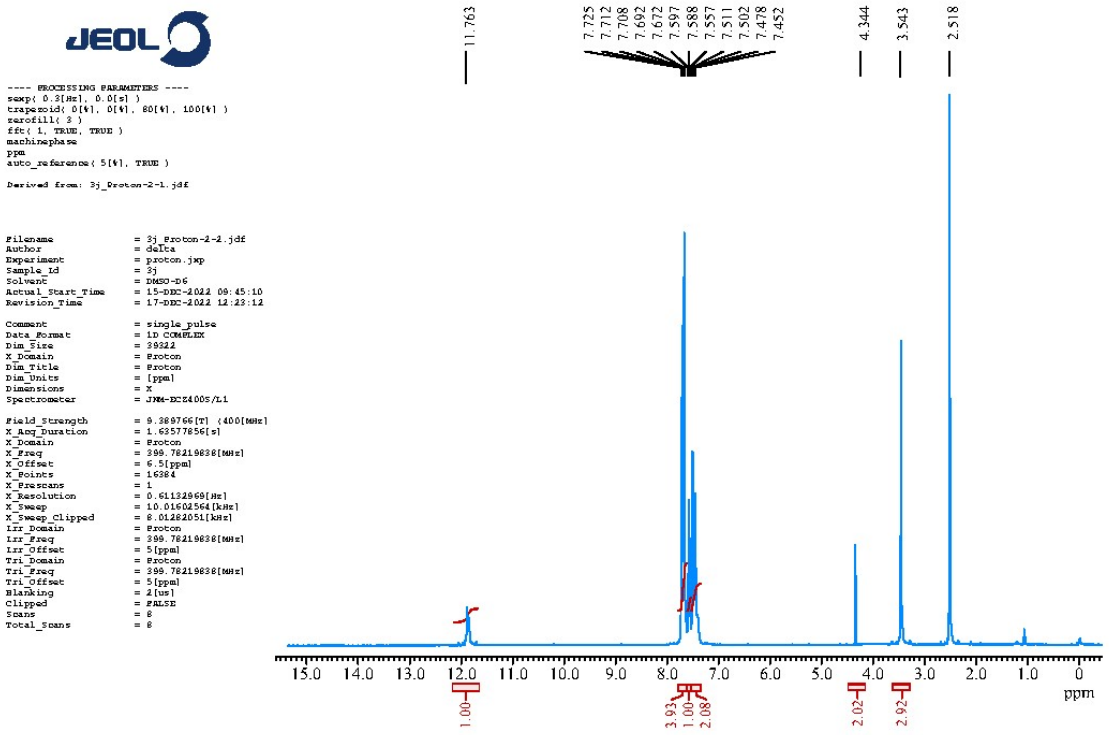


(Z)-N-(3-Chloro-2-methylphenyl)-2-(2,4-dioxo-5-(thiophen-2-ylmethylene)thiazolidin-3-yl)acetamide (3j):yellow solid, yield 77%, MP 224–226 °C, FTIR (KBr, cm−1): 3474.54 (NH), 3032.81 (Ar C–H), 1733.63 (C=O), 1158.37 (C-N). 1H-NMR (δ ppm, DMSO-*d6*): 3.543 (s, 3H, CH_3), 4.344 (s, 2H, CH_2), 7.452-7.725 (m, 8H, Ar-H), 11.763 (s, 1H, NH). 13C-NMR (δppm, DMSO-*d6*): 30.45, 55.49, 100.02, 112.44, 115.28, 120.21, 120.27, 129.00, 129.06, 131.27, 137.59, 144.60, 144.71, 147.38, 153.38, and 164.63. MS (m/z): M+ analyzed392.0101, M+ predicted 392.0052.

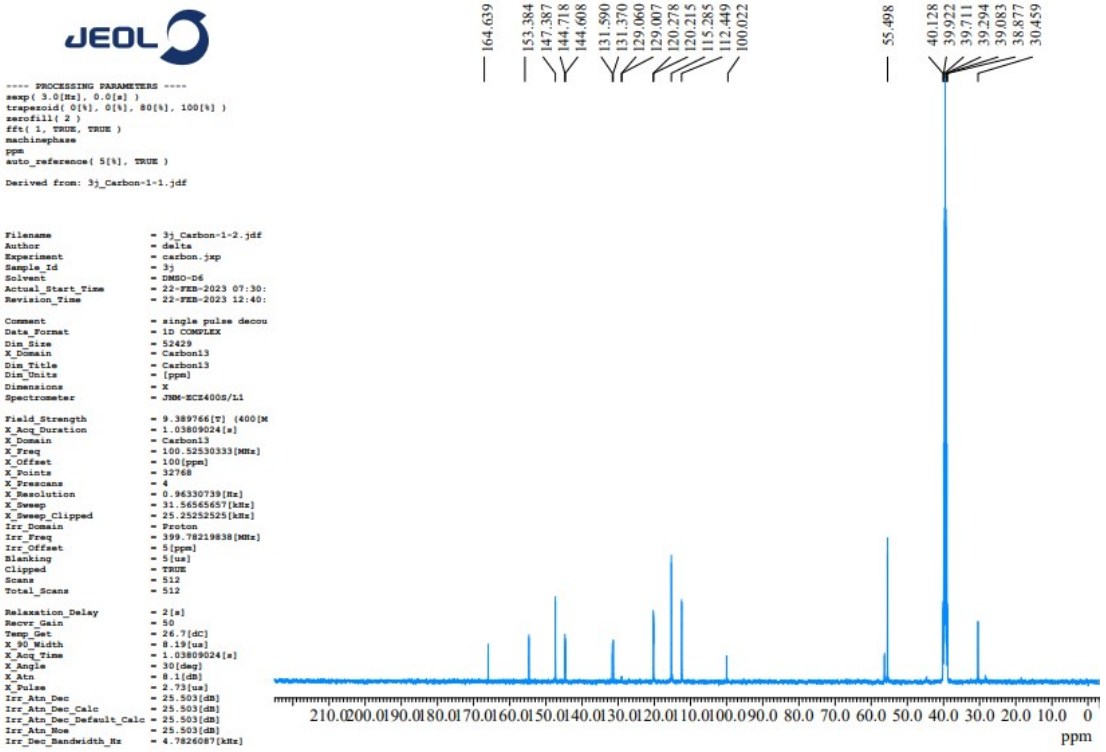
(Z)-N-(3-Chloro-2-methylphenyl)-2-(2,4-dioxo-5-(thiophen-2-ylmethylene)thiazolidin-3-yl)acetamide (3j):



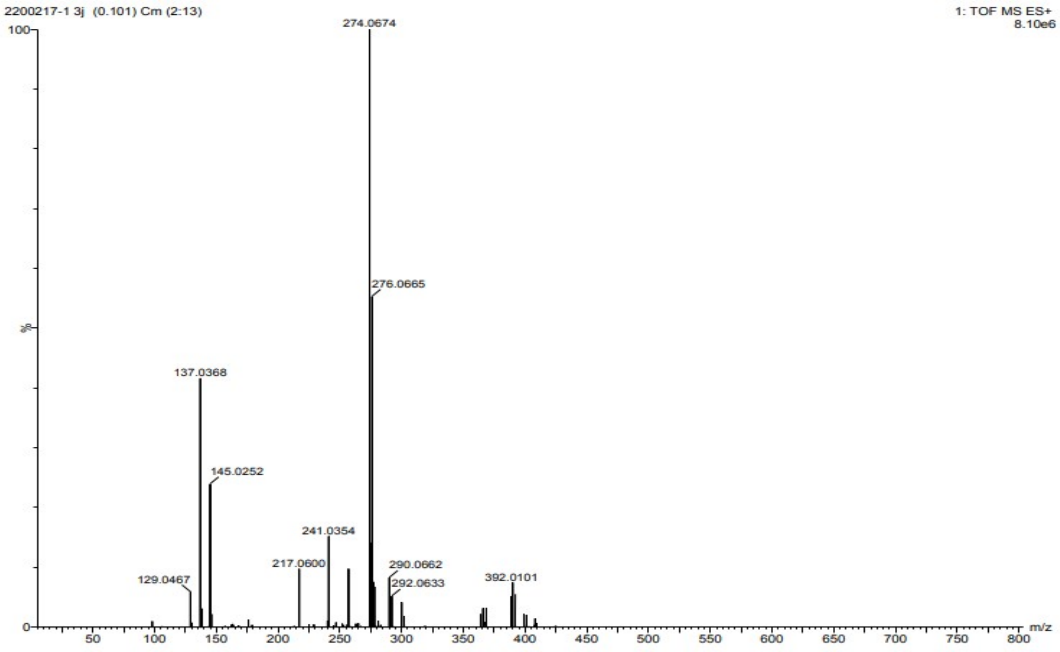
(Z)-N-(3-Chloro-2-methylphenyl)-2-(2,4-dioxo-5-(thiophen-2-ylmethylene)thiazolidin-3-yl)acetamide(3j):



(Z)-N-(3-Chloro-2-methylphenyl)-2-(2,4-dioxo-5-(thiophen-2-ylmethylene)thiazolidin-3-yl)acetamide(3j):



(Z)-N-(3-Chloro-2-methylphenyl)-2-(2,4-dioxo-5-(thiophen-2-ylmethylene)thiazolidin-3-yl)acetamide (3j):



Ethical approval

NITTE (Deemed to be University) | NGSM INSTITUTE OF PHARMACEUTICAL SCIENCES

(Established under Section 3 of UGC Act, 1956)
Placed under Category 'A' by MHRD, GoI, Accredited with 'A' Grade by NAAC

Ref: NGSM/IAEC/2020-21/220

Date: 29th Dec 2020

To

Mr. Mahendra G. S.
Research Scholar
NGSMIPS
Paneer, Deralakatte - 575 018

Sub: Approval of protocol by IAEC

The Institutional Animal Ethics Committee of NGSM Institute of Pharmaceutical Science has approved your protocol for experimentation on small animals for the project titled "Design synthesis of novel thiazolidinedione and rhodanine for antidiabetic activity" during the meeting held on 29th December, 2020. Approval number of your protocol is **NGSMIPS/IAEC/DEC-2020/219**.

Chairman and Scientist In-charge of Animal House Facility
Dr. C. S. Shastry
Principal

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