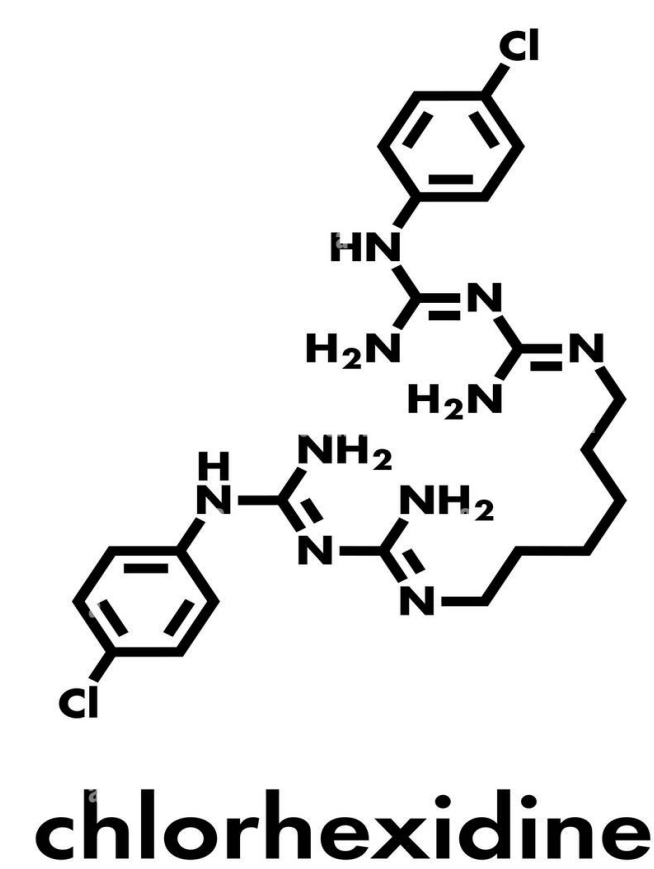


Introduction

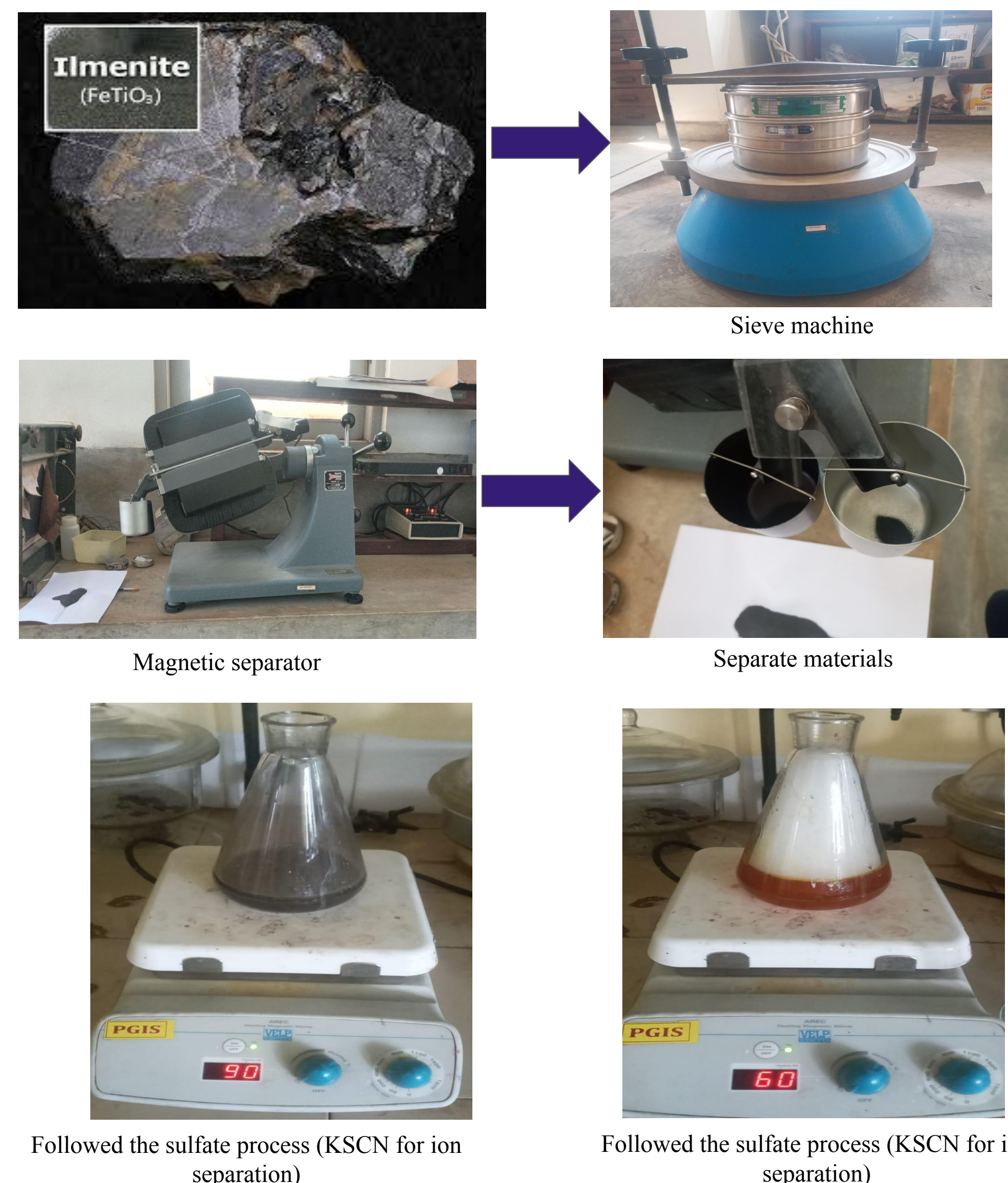
- Ilmenite (FeTiO₃) is a naturally available mineral rich in iron (Fe) and titanium (Ti) sources.
- It is a low-cost, naturally abundant, and environmentally friendly material that has been identified as a promising precursor for biomedical applications.
- Fe₂O₃NPs were synthesized through acid leaching using hydrochloric or sulfuric acid, while TiO₂NPs were prepared via the sulfate process using H₂SO₄ leaching.
- Chlorhexidine (CHX), an antimicrobial and antiplaque agent, was incorporated into synthesized drug loaded NPs by using two drug-loading techniques: incipient wetness impregnation (IWI) and absorption equilibrium (AE) methods.
- In vitro drug release studies were conducted by the dialysis method in both acidic (pH 5.5) and neutral (pH 7.4) medium to study their drug releasing and their kinetics models.



Objective: This study aims to select the most effective CHX drug-loaded naturally synthesised nanoparticles from Ilmenite for controlled drug delivery. For that, the natural Ilmenite is used to synthesize Fe₂O₃NPs and TiO₂NPs, optimize CHX drug loading using two techniques (incipient wetness impregnation (IWI) and absorption equilibrium (AE)), and investigate their *in vitro* drug release profiles under different pH conditions and further analysis based on drug release kinetic models.

Methodology

Fe₂O₃NPs and TiO₂NPs synthesis process



Drug Loading experiments

1. Absorption Equilibrium (AE)

Adding 125 mg of synthesized NPs to a 2% CHX solution in IPA by 1:1 ratio

Stirring for 24 hours

Measuring the absorbance of supernatant at 260 nm

In vitro drug release

Dispersing 50 mg of CHX loaded NPs in 100 ml of PBS solution

Shaking to ensure proper mixing

Measuring the absorbance at 260 nm at one-hour intervals for 52 hours

Studying kinetics drug release models

2. Incipient Wetness impregnation (IWI)

Adding dropwise 2% CHX/ IPA solution to 125 mg of synthesized NPs

Maintaining 37 °C for dry particles

CHX encapsulation efficiency (EE)

$$EE = \left\{ \frac{\text{Initial CHX concentration} - \text{free CHX concentration}}{\text{Initial CHX concentration}} \right\} \times 100$$

Results

Characterization of Fe₂O₃ Nanoparticles

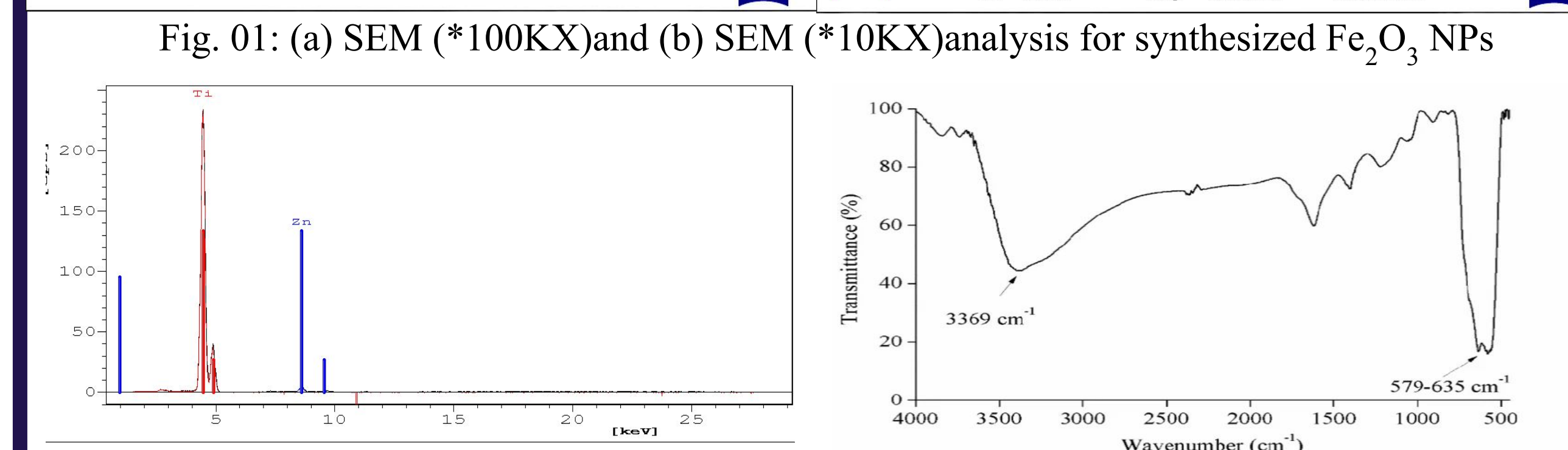
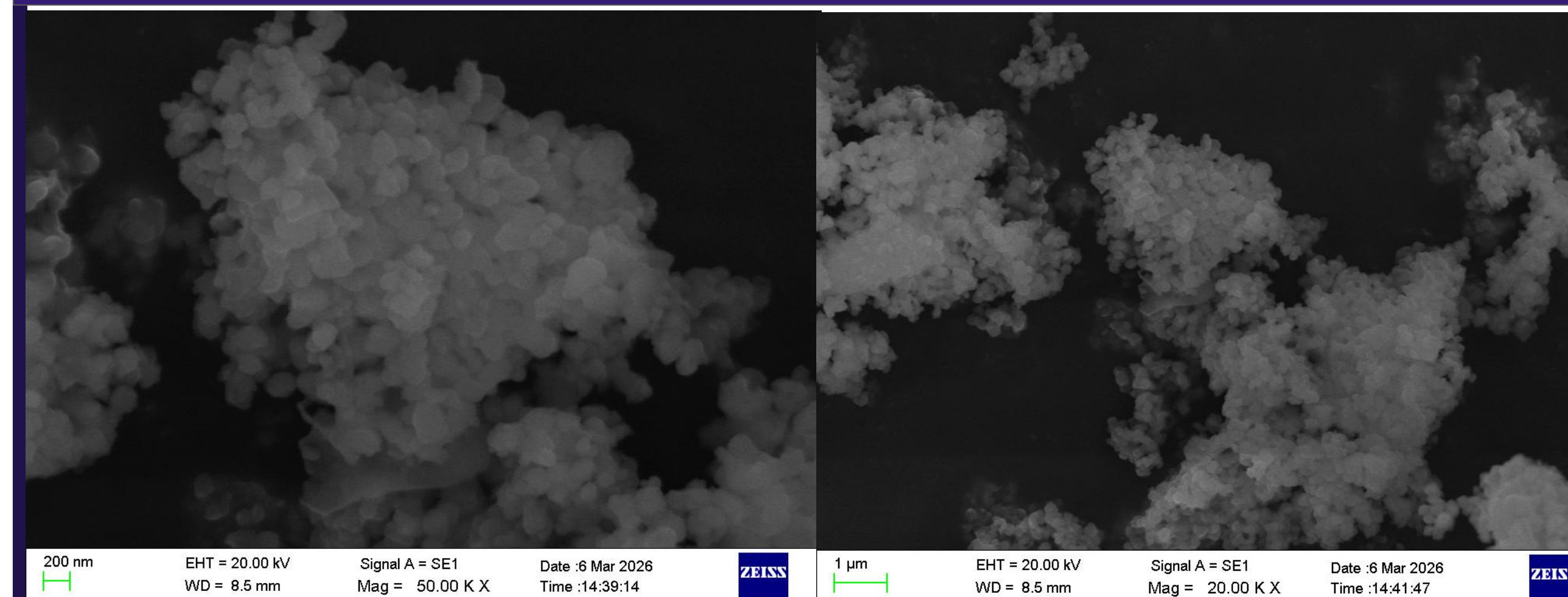


Fig. 02: (a) XRF and (b) FTIR analysis for synthesized nanoparticles

Characterization of TiO₂ Nanoparticles

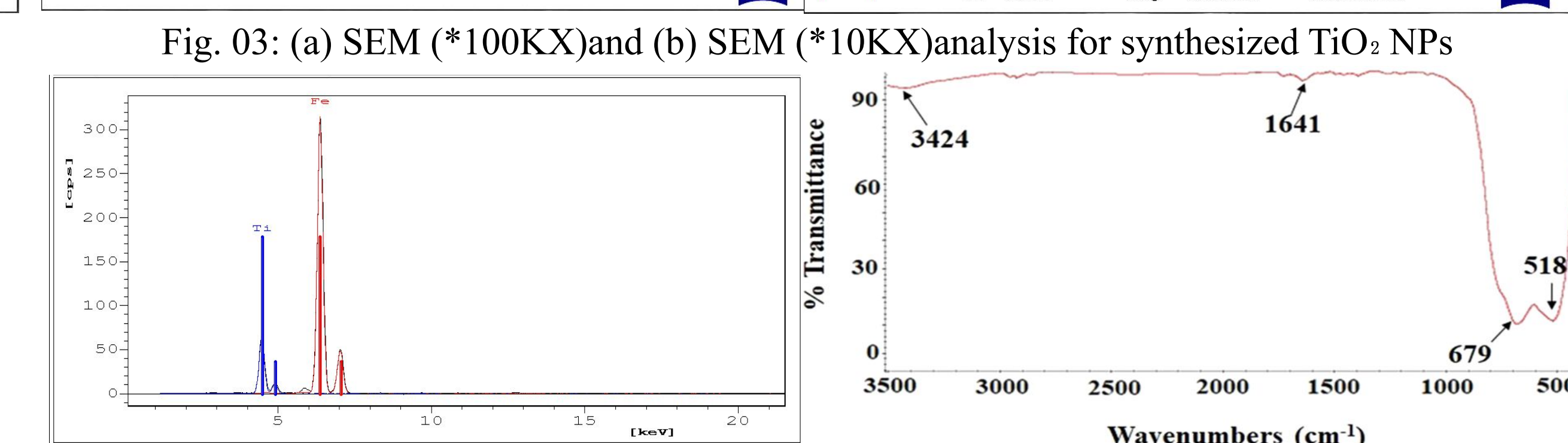
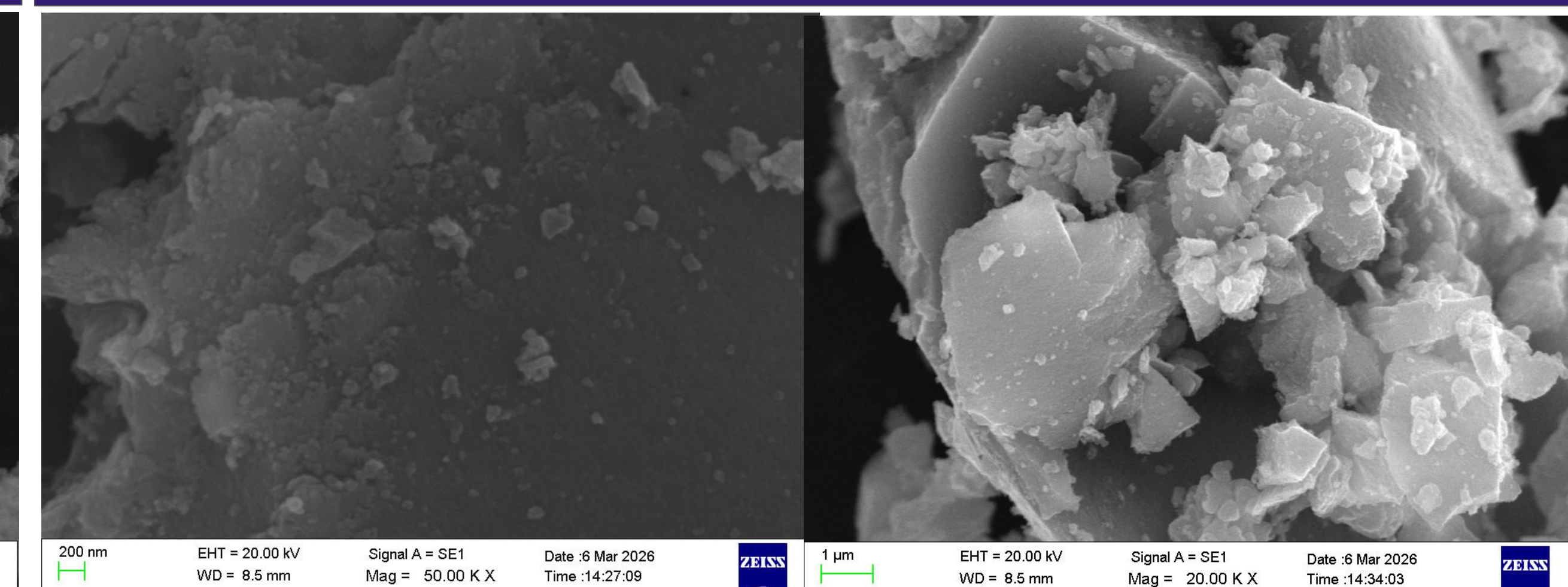
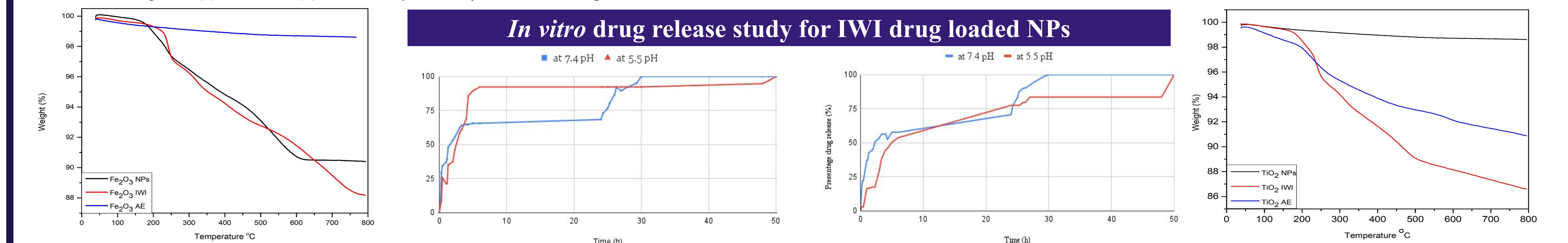


Fig. 04: (a) XRF and (b) FTIR analysis for synthesized nanoparticles

In vitro drug release study for IWI drug loaded NPs



Discussion

- The results confirmed the successful synthesis of high-quality nanoparticles, with Fe₂O₃NPs (87.5 nm) and TiO₂NPs (48.6 nm) showing characteristic Fe–O, Fe–O–C, and Ti–O–Ti bonds along with CHX binding peaks in FTIR analysis, while EDXRF confirmed the absence of hazardous elemental impurities.
- The drug entrapment efficiency for Fe₂O₃ nanoparticles was 48.4% when prepared using the IWI method, compared to 20.25% using the AE method. For TiO₂ nanoparticles, the entrapment efficiency was 49.6% for IWI and 30.16% for AE.
- The drug loading capacity determined by TGA for Fe₂O₃ nanoparticles was 10.42% for IWI and 8.2% for AE. In the case of TiO₂ nanoparticles, the loading capacity was 12.03% for IWI and 7.74% for AE.

Conclusion

CHX-loaded TiO₂ nanoparticles prepared using the IWI method demonstrated the highest drug-loading capacity and exhibited pH-responsive sustained release behavior, indicating strong potential for oral drug delivery applications.

Reference

- Rajakaruna, T. P. B.; Udawatte, C. P.; Chandrajith, R.; Rajapakse, R. M. G. Formulation of Iron Oxide and Oxy-Hydroxide Nanoparticles from Ilmenite Sand through a Low-Temperature Process. *ACS Omega* 2021, 6 (28), 17824–17830. <https://doi.org/10.1021/acsomega.1c09938>.
- Chen, X.; Mao, S. S. Titanium Dioxide Nanomaterials: Synthesis, Properties, Modifications, and Applications. *ChemInform* 2007, 38 (41). <https://doi.org/10.1002/chin.200741216>.
- Peppas, N. Hydrogels in Pharmaceutical Formulations. *European Journal of Pharmaceutics and Biopharmaceutics* 2000, 50 (1), 27–46. [https://doi.org/10.1016/S0939-6411\(00\)00090-4](https://doi.org/10.1016/S0939-6411(00)00090-4).

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