Brazilian Journal of Experimental Design, Data Analysis and Inferential Statistics

Federal University of Rio de Janeiro

BJEDIS, Rio de Janeiro, 2023 – 2 YEARS BJEDIS , v. 01 (1), 2023

DOI: https://doi.org/10.55747/bjedis.v1i1.62207

ISSN: 2763-6925

Received 05/12/2023. Revised 11/12/2023. Accepted 13/12/2023. Published 15/12/2023.

Comparative Analysis of Sibutramine Concentration Determination: Gravimetric Methods vs. FTIR RMSE Technique in Pharmaceutical Compositions

Fernando Gomes [a,b] and Maria Verônica Freitas [a]

[a.] Instituto de Macromoléculas Professora Eloisa Mano, Centro de Tecnologia-Cidade Universitária, Universidade Federal de Rio de Janeiro, Rio de Janeiro, Brazil fgsj@ufrj.br

[b] Programa de Engenharia da Nanotecnologia, COPPE, Centro de Tecnologia-Cidade Universitária, Universidade Federal do Rio de Janeiro, Rio de Janeiro. Brazil

Abstract

This paper underscores the practical implications of employing FTIR RMSE analysis in pharmaceutical research. It highlights the method's rapid and non-destructive nature for quantifying drug concentration in complex formulations, emphasizing its significance in pharmaceutical quality assurance. The study advocates for integrating FTIR RMSE with conventional gravimetric and volumetric methods to enhance the analytical toolkit for pharmaceutical compound analysis. Furthermore, it elucidates the potential of FTIR RMSE in expediting analytical processes and improving estimation accuracy. The paper accentuates the synergy between classical gravimetric techniques and modern spectroscopic methods, providing valuable insights into pharmaceutical compound analysis within heterogeneous formulations. In terms of contributions, this paper advances analytical methods in pharmaceutical research by comprehensively exploring traditional gravimetric/volumetric techniques alongside Fourier Transform Infrared Spectroscopy (FTIR) coupled with Root Mean Square Error (RMSE) analysis. It assesses their effectiveness in determining drug concentrations, mainly focusing on sibutramine quantification, a complex active pharmaceutical ingredient. The results indicate a strong correlation (R^2 = 0.987) between the two methodologies, with FTIR RMSE consistently yielding slightly higher results due to its sensitivity to molecular structural fluctuations and component interactions. In conclusion, this study advocates for integrating FTIR RMSE into pharmaceutical research practices. It emphasizes the need for calibration and refinement of this technique to further enhance estimation accuracy and analytical precision. It underscores the pivotal role of advanced analytical methods in various applications, including pharmaceutical and biomedical fields.

Keywords: Pharmaceutical research, analytical methods, gravimetric methods, volumetric methods, Fourier Transform Infrared Spectroscopy (FTIR), Root Mean Square Error (RMSE) analysis, sibutramine quantification, drug concentration determination, correlation, reliability, rapid analysis, non-destructive analysis, pharmaceutical quality assurance, spectroscopic techniques, compound analysis.

* Correspondence address for this author of the Department of Macromolecules Professor Eloisa Mano, Polymer Science and Technology Faculty, Federal University of Rio de Janeiro, CEP: 21941-598, City: Rio de Janeiro, Country: Brazil; Email: fgsj74@gmail.com

Adherence to the BJEDIS' scope: The presented work aligns seamlessly with the Brazilian Journal of Experimental Design, Data Analysis, and Inferential Statistics (BJEDIS) scope. It centers on analytical methodologies within pharmaceutical research, specifically the application of Fourier Transform Infrared Spectroscopy (FTIR) and Root Mean Square Error (RMSE) analysis. This alignment is rooted in the empirical nature of the research, emphasizing its role in advancing applied statistical knowledge. Furthermore, the study effectively fulfills the journal's mission of informing researchers and professionals about the prevailing trends in Experimental Design, Data Analysis, and Inferential Statistics. This work aligns with BJEDIS' core objective of knowledge dissemination and highlights the practical relevance of the work to the academic and scientific community. The paper's interdisciplinary nature, spanning Sciences and Engineering, notably reflects the journal's inclusive approach. This convergence of expertise makes it a pertinent and valuable addition to BJEDIS, furthering its mission of providing a platform for comprehensive and relevant research contributions.

1. INTRODUCTION

The field of pharmaceutical research and polymer materials has witnessed significant progress in analytical and characterization methodologies (1–10). Two notable techniques, Fourier Transform Infrared Spectroscopy (FTIR) and Root Mean Square Error (RMSE) analysis have emerged as crucial tools for evaluating the composition and attributes of diverse systems (11–13).

Recent investigations have prominently employed RMSE analysis via FTIR to assess the efficacy of polymeric systems in various applications such as oil absorption, bioremediation, and controlled drug release (11–17) .

The study by Ferreira et al. (2012) (17) delves into oil absorbents based on CNSL, furfural, and lignin, showcasing their chemical resemblance to petroleum for improved absorption. FTIR-RMSE was pivotal in quantifying this chemical similarity, facilitating precise formulation adjustments for optimal efficiency.

Grance et al. (2012) (15) developed magnetic nanocomposites tailored for oil absorption, emphasizing their effectiveness and magnetic attributes. The incorporation of FTIR-RMSE in their research allowed for a meticulous analysis of the interaction between magnetic nanoparticles and resin, affirming the viability of this approach for environmental remediation.

Caetano et al. (2018) (16) shed light on gamma-irradiated poly(butylene succinate) (PBS) as a tool for oil spill bioremediation. The material's capacity to immobilize nutrients opens new horizons for environmental cleanup, with FTIR-RMSE analysis effectively assessing the controlled release of these nutrients, a critical aspect of biodegradation.

Figueiredo et al. (2019) (14) introduced extrinsically magnetic PBS as a novel solution for oil spill remediation. FTIR-RMSE analysis played a crucial role in validating the efficacy of the cleaning process, demonstrating the material's ability to absorb oil under practical conditions.

Pereira et al. (2013) (11) investigated the influence of magnetic fields and maghemite nanoparticles on drug dissolution in PLGA nanocomposites. FTIR-RMSE proved instrumental in mapping the dissolution profile of cotrimoxazole, offering profound insights into the impact of magnetic fields and nanoparticles on drug release.

Pereira et al. (2016) (12) centered their research on the release of oxaliplatin from PLGA and PLGA-PEG matrices, highlighting the positive influence of PEG on drug release. FTIR-RMSE significantly contributed to the analysis of dissolution profiles, shedding light on how polymeric modifications can enhance chemotherapy therapies.

Ferreira et al. (2017) (13) explored the modification of PBS with rutin to enhance the release of silybin, showcasing the potential of natural compounds as chain extenders. The utilization of FTIR-RMSE provided intricate insights into the resulting molecular changes, a crucial aspect for comprehending and optimizing drug release.

In all these instances, FTIR-RMSE has emerged as an indispensable analytical tool, enabling a comprehensive evaluation of polymer and composite properties. It has deepened our understanding of material compositions and their chemical resemblances to target substances, enhancing our comprehension of the associated phenomena.These studies underscore the potential of modified polymeric materials and the significance of advanced analytical methods in comprehending their characteristics.

This study is centered on applying these innovative techniques to scrutinize the concentration of sibutramine in different pharmaceutical compositions, comparing them to conventional gravimetric and volumetric approaches. Sibutramine, a pivotal active compound in numerous pharmaceutical

By scrutinizing the applicability and precision of FTIR RMSE analysis for quantifying drug concentrations, this study substantially contributes to the progression of analytical methods within pharmaceutical research. Furthermore, it aims to furnish valuable insights into adopting advanced spectroscopic techniques compared to conventional methodologies, with the potential to augment analytical practices and enhance quality assurance standards in the pharmaceutical and biomedical realms.

Methodology

In the methodology employed for this study, the initial step involved material preparation. This process comprised dissolving sibutramine in methanol and diluting it with a chitosan solution, creating three distinct samples.

Sample R6 consisted of sibutramine appropriately diluted within the chitosan solution. Sample R7 involved the introduction of sodium tripolyphosphate (Tpp) and a precise addition of 25% mango fiber relative to the chitosan's mass. Sample R8, on the other hand, incorporated Tpp and a precise 50% mass addition of mango fiber concerning the chitosan component.

The study employed Root Mean Square Error (RMSE) and Fourier Transform Infrared Spectroscopy (FTIR) analysis following material preparation. The samples underwent FTIR analysis using the attenuated total reflection (ATR) technique. This analytical approach utilized a Perkin-Elmer 1720X Fourier-transform spectrometer, with results reported as averages based on 24 scans conducted over the 4000–675 cm^{-1} range.

Linear regression and the least squares method were employed for statistical analyses of sample transmissions. These analytical tools enabled the determination of critical correlation values (R2) and root mean square error (RMSE) of dispersion, offering insights into data consistency and accuracy.

Specialized software was utilized to estimate the percentage of sibutramine present in the samples via RMSE analysis. The software employed a linear interpolation approach, comparing RMSE values from FTIR analyses with those derived from a reference sample - an unmodified PBS. The hypothesis underlying this methodology posited that differences in RMSE values between the samples and the reference sample proportionally reflected changes in drug concentration.

The software, designed for precision and accuracy, leveraged Python's NumPy library to process and analyze spectroscopic data. It executed several essential functions, each with a specific role in the analytical process.

Initially, the software facilitated the creation of a structured RMSE value matrix containing RMSE data for various samples. Each row represented a distinct sample, while columns enabled comparisons between each sample and the reference sibutramine sample (SIB).

Indices were defined to distinguish between 0% and 100% drug samples. 'Indices_0_percent' categorized samples lacking the drug, such as chitosan and tripolyphosphate, while 'index_100_percent' pertained to the reference sample containing 100% drug concentration (SIB).

Additionally, the software computed an average RMSE for drug-free samples labeled 'avg_rmse_0_percent.' This average was determined based on RMSE values obtained from the drug-free samples compared to the pure sibutramine sample (SIB).

The core function of the software was 'estimate_drug_percentage,' which employed RMSE data to estimate the drug's percentage within a given sample. This function employed a linear interpolation formula, calculating the percentage relative to the difference between the sample's RMSE value concerning SIB and the average RMSE of drug-free samples. This calculation was conducted proportionally to the RMSE difference observed for the 100% drug sample (SIB), ensuring non-negative estimated percentages.

Subsequently, the software was utilized to estimate the drug's percentage within specific samples, namely R6, R7, and R8, employing the previously described function. The resulting values were computed based on the respective RMSE values compared to the SIB sample.

Ultimately, the software concluded its operation by presenting the estimated drug percentages for samples R6, R7, and R8, offering valuable quantitative insights into the drug concentration within these complex samples.

Results and Discussions

The investigation involved a meticulous assessment of sibutramine concentration within various samples, employing gravimetric methods and RMSE (Root Mean Square Error, see Table 1) analysis via Fourier Transform Infrared Spectroscopy (FTIR, See Figure 1).

The FTIR spectra in Figure 1 portray a range of curves, each representing the infrared transmittance for different sample sets, including sibutramine, composite compositions, and materials like chitosan and tripolyphosphate. The information conveyed by these spectra is as follows:

In the spectral range of 4000-2500 cm^{-1}, known as the O-H and N-H stretching region, a broad absorption peak around 3300 cm^{-1} indicates O-H stretching vibrations, suggesting the presence of alcohols, phenols, or water. Additionally, N-H stretching bands may be present in cases like sibutramine.

Moving to the 2500-2000 cm^{-1} region, there are typically few spectral bands and distinctive features are generally absent.

In the 2000-1500 cm^{-1} region, associated with C=O and C=C stretching vibrations, strong bands at approximately 1700 cm^{-1} represent carbonyl C=O group stretching vibrations, commonly found in compounds like aldehydes, ketones, carboxylic acids, and esters. Bands around 1600 cm^{-1} may indicate C=C bond stretching vibrations, often in aromatic rings or unsaturated alkyl chains.

Entering the 1500-1000 cm^{-1} region, characterized by C-O stretching and C-H bending vibrations, bands within this interval may signify various vibrational modes, including C-H bending and C-O stretching, typical of compounds such as ethers, alcohols, and carboxylic acids. A distinct band near 1100 cm^{-1} may suggest C-O-C stretching vibrations commonly associated with ethers or esters.

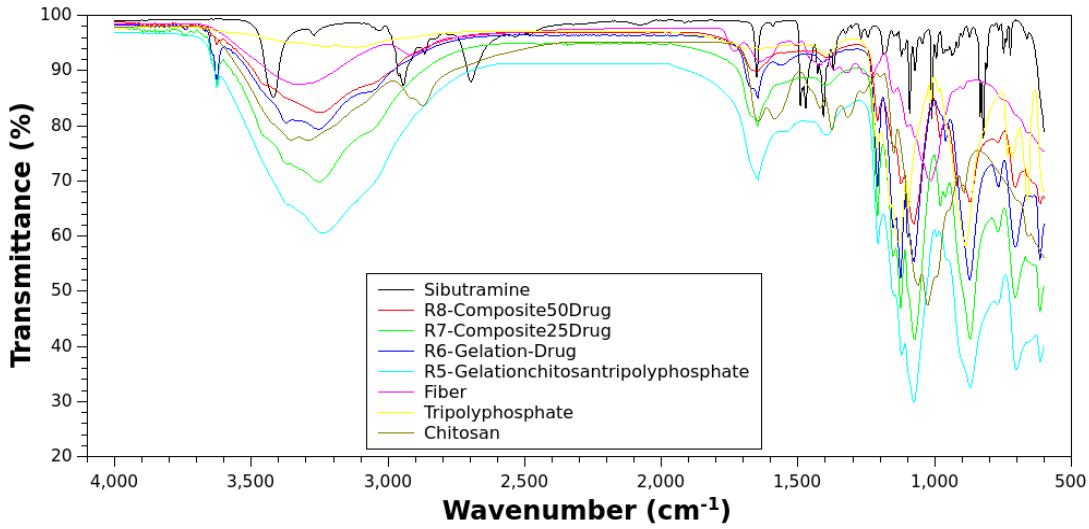

Figure 1 – FTIR spectra of the samples

Finally, below 1000 cm^{-1} , the spectral domain offers intricate details but is often congested, interpreting challenging without specific reference points.

It is crucial to recognize that differences between the curves for each sample reflect variations in chemical composition. Notably, the curves representing composites R6-R8 show significant deviations compared to pure sibutramine and other materials. These differences suggest chemical interactions or physical alterations resulting from the integration of the drug into the composites. Understanding these dynamics is essential for comprehending sibutramine's interactions with other constituents in the composites and their potential impact on the final material properties.

RMSE values in Table 1 follow the sequence C (Chitosan), T (Tripolyphosphate), F (Fiber), R5 (Gelation (chitosan & tripolyphosphate)), R6(Gelation-Drug), R7(Composite (25% & Drug)), R8(Composite (50% & Drug)), and S (Sibutramine)

Table 1 – RMSE values

Sample	C	T	F	R5	R6	R7	R8	S
C	0	15.9	4.6	11.8	13.4	12.2	11.4	14.8
T	16.1	0	15.3	13.9	10.9	12.8	12	15.6
F	4.89	16	0	13	13.9	13	12.3	14.9
R5	10	11.6	10.4	0	5.47	3.24	3.58	15.3
R6	12.5	10.1	12.2	6.03	0	3.54	4.52	15.5
R7	10.8	11.1	10.8	3.37	3.34	0	2.31	15.4
R8	10.5	10.8	10.6	3.86	4.43	2.4	0	15.3
S	20.3	21.1	19.3	24.7	22.7	23.9	22.9	0

These RMSE data were calculated using this software:

```
import numpy as np

# RMSE values matrix
rmse_values = np.array([
    [0, 15.9, 4.6, 11.8, 13.4, 12.2, 11.4, 14.8],   # Chitosan
    [16.1, 0, 15.3, 13.9, 10.9, 12.8, 12, 15.6],    # Tripolyphosphate
    [4.89, 16, 0, 13, 13.9, 13, 12.3, 14.9],        # Fiber
    [10, 11.6, 10.4, 0, 5.47, 3.24, 3.58, 15.3],    # R5
    [12.5, 10.1, 12.2, 6.03, 0, 3.54, 4.52, 15.5],  # R6
    [10.8, 11.1, 10.8, 3.37, 3.34, 0, 2.31, 15.4],  # R7
    [10.5, 10.8, 10.6, 3.86, 4.43, 2.4, 0, 15.3],   # R8
    [20.3, 21.1, 19.3, 24.7, 22.7, 23.9, 22.9, 0]   # SIB
])

# Indices for 0% and 100% drug samples
indices_0_percent = [0, 1, 2, 3]  # Chitosan, Tripolyphosphate, Fiber, R5
index_100_percent = 7  # SIB

# Calculate the average RMSE of 0% drug samples relative to SIB
avg_rmse_0_percent = np.mean(rmse_values[indices_0_percent, index_100_percent])

# Function to estimate drug percentage using RMSE relative to SIB
def estimate_drug_percentage(rmse_sample_to_SIB, avg_rmse_0, rmse_100):
    # Linear interpolation formula with non-negative constraint
    percentage = 100 * (rmse_sample_to_SIB - avg_rmse_0) / (avg_rmse_0 - rmse_100)
    return max(percentage, 0)  # Ensure non-negative percentages

# Estimating drug percentages for R6, R7, R8
drug_percentage_R6 = estimate_drug_percentage(rmse_values[4, index_100_percent], avg_rmse_0_percent,
rmse_values[index_100_percent, index_100_percent])
drug_percentage_R7 = estimate_drug_percentage(rmse_values[5, index_100_percent], avg_rmse_0_percent,
rmse_values[index_100_percent, index_100_percent])
drug_percentage_R8 = estimate_drug_percentage(rmse_values[6, index_100_percent], avg_rmse_0_percent,
rmse_values[index_100_percent, index_100_percent])

print(f"Estimated drug percentage in R6: {drug_percentage_R6:.2f}%")
print(f"Estimated drug percentage in R7: {drug_percentage_R7:.2f}%")
print(f"Estimated drug percentage in R8: {drug_percentage_R8:.2f}%")
```

A comparative evaluation of the results obtained from both methods reveals their consistency and precision. Table 2 presents the results.

Table 2 – Comparison between methods

Method	Sample R6 (%)	Sample R7 (%)	Sample R8 (%)
Gravimetric Methods	1.00	0.80	0.67
FTIR RMSE Analysis	2.31	1.65	0.99

The results reveal a strong correlation between the two methodologies, with an R^2 value of 0.987. This robust correlation suggests that despite variations in absolute percentage values, both methods exhibit consistent trends.

However, a notable difference arises in the absolute percentage values, where FTIR RMSE consistently yields higher results than gravimetric methods. This discrepancy is attributed to the distinct characteristics of the techniques. FTIR excels in detecting molecular structural fluctuations and component interactions, while gravimetric methods offer direct material quantity measurements.

A closer examination reveals a significant trend – decreased sibutramine concentration from Sample R6 to Sample R8. This underscores the effectiveness of the FTIR RMSE technique in distinguishing and quantifying the drug in the compositions.

These findings highlight the value of the FTIR RMSE technique, which provides speed and non-destructive analysis in estimating sibutramine concentrations in complex pharmaceutical formulations. However, calibration with known standards is advised to enhance precision and address observed differences in absolute values.

In conclusion, this comprehensive comparative analysis underscores the effectiveness of the FTIR RMSE technique for determining sibutramine concentration in complex matrices. It demonstrates the benefits of combining traditional analytical methods with advanced spectroscopic techniques in pharmaceutical compound analysis across diverse formulations.

Conclusions

In conclusion, this comprehensive study has conducted a meticulous comparative analysis, pitting traditional gravimetric methods against the advanced RMSE (Root Mean Square Error) FTIR technique to quantify sibutramine concentration in various pharmaceutical compositions. The resulting insights can be summarized as follows:

The analysis reveals a robust correlation, with an R^2 value of 0.987, indicating a harmonious agreement between gravimetric methods and FTIR RMSE analysis, transcending the intricacies of absolute percentage values. This strong consistency underscores the reliability of both analytical approaches, emphasizing their shared ability to discern underlying trends.

Furthermore, the FTIR RMSE technique exhibits heightened sensitivity to molecular structure fluctuations and component interactions, resulting in slightly higher percentage values than gravimetric methods. This observation highlights the importance of selecting the appropriate analytical technique tailored to the specific characteristics of the compound under scrutiny.

Beyond validation, this study champions the practicality of the FTIR RMSE technique. It is a rapid and non-destructive method for determining drug concentration in complex pharmaceutical formulations. This practicality holds significant implications for pharmaceutical research, where expediency and precision are paramount.

Looking ahead, the study calls for the calibration and refinement of the FTIR RMSE technique to enhance estimation accuracy. This endeavor opens new horizons for future research, guiding the path toward heightened analytical precision and methodological refinement.

In the broader context of pharmaceutical research, this study underscores the synergy between classical methodologies and modern spectroscopic techniques. The amalgamation of these approaches enhances the analysis of pharmaceutical compounds within heterogeneous formulations, providing deeper insights and analytical prowess.

This study delivers a resounding message to analytical practices—embrace the symbiosis of gravimetric methods and FTIR spectroscopy. This nexus of formidable techniques should be enshrined, particularly in analytical scenarios demanding precision and sensitivity. It serves as a safeguard, upholding product quality and safety sanctity.

Acknowledgments:
The authors extend their appreciation to the following organizations for their invaluable funding and scholarship provisions: Agência Nacional de Petróleo (ANP), Conselho Nacional de Desenvolvimento Científico e Tecnológico (CNPq), Coordenação de Aperfeiçoamento de Pessoal de Nível Superior (CAPES), and Fundação Carlos Chagas Filho de Amparo à Pesquisa do Estado do Rio de Janeiro (FAPERJ). Their unwavering support was instrumental in realizing this research endeavor.

Funding: This research received generous backing from Agência Nacional de Petróleo (PRH 16.1), Conselho Nacional de Desenvolvimento Científico e Tecnológico (CNPq BRICS-STI-5440090/2022-9 and PQ-2022302508/2022-8), Coordenação de Aperfeiçoamento de Pessoal de Nível Superior (CAPES - Finance Code 001), and Fundação Carlos Chagas Filho de Amparo à Pesquisa do Estado do Rio de Janeiro (FAPERJ E-26/210.800/2021(Energy), E-26/211.122/2021 (COVID), E-26/210.511/2021 (ConBraPA2022), e-26/201.154/2021 (CNE) and E-S26/210.080/2023 (Thematic)).

References

1. LI, Wanqing, ZHENG, Nan, ZHOU, Qiang, ALQAHTANI, Mohammed S., ELKAMCHOUCHI, Dalia H., ZHAO, Huajun and LIN, Sen. A state-of-the-art analysis of pharmacological delivery and artificial intelligence techniques for inner ear disease treatment**. Environmental Research**. v. 236, p. 116457. 2023.

2. SHAH, Birju, KAKUMANU, Vasu Kumar and BANSAL, Arvind K. Analytical techniques for quantification of amorphous/crystalline phases in pharmaceutical solids**. Journal of pharmaceutical sciences**. v. 95, n. 8, p. 1641–1665. 2006.

3. SIDDIQUI, Masoom Raza, ALOTHMAN, Zeid A. and RAHMAN, Nafisur. Analytical techniques in pharmaceutical analysis: A review**. Arabian Journal of chemistry**. v. 10, p. S1409–S1421. 2017.

4. AZIZ, Tariq, ULLAH, Asmat, ALI, Amjad, SHABEER, Muhammad, SHAH, Muhammad Naeem, HAQ, Fazal, IQBAL, Mudassir, ULLAH, Roh and KHAN, Farman Ullah. Manufactures of bio-degradable and bio-based polymers for bio-materials in the pharmaceutical field**. Journal of Applied Polymer Science**. v. 139, n. 29, p. e52624. 2022. DOI 10.1002/app.52624.

5. KOVARIK, Michelle L., GACH, Philip C., ORNOFF, Douglas M., WANG, Yuli, BALOWSKI, Joseph, FARRAG, Lila and ALLBRITTON, Nancy L. Micro Total Analysis Systems for Cell Biology and Biochemical Assays**. Analytical Chemistry**. v. 84, n. 2, p. 516–540. 2012. DOI 10.1021/ac202611x.

6. WHITCOMBE, Michael J., KIRSCH, Nicole and NICHOLLS, Ian A. Molecular imprinting science and technology: a survey of the literature for the years 2004-2011: MOLECULAR IMPRINTING SCIENCE AND TECHNOLOGY: 2004-2011**. Journal of Molecular Recognition**. v. 27, n. 6, p. 297–401. 2014. DOI 10.1002/jmr.2347.

7. VEHRING, Reinhard. Pharmaceutical Particle Engineering via Spray Drying**. Pharmaceutical Research**. v. 25, n. 5, p. 999–1022. 2008. DOI 10.1007/s11095-007-9475-1.

8. JAYARAMAN, Krishnan, KOTAKI, M., ZHANG, Yanzhong, MO, Xiumei and RAMAKRISHNA, S. Recent advances in polymer nanofibers**. Journal of Nanoscience and Nanotechnology**. v. 4, n. 1–2, p. 52–65. 2004.

9. KOLE, Prashant Laxman, VENKATESH, Gantala, KOTECHA, Jignesh and SHESHALA, Ravi. Recent advances in sample preparation techniques for effective bioanalytical methods**. Biomedical Chromatography**. v. 25, n. 1–2, p. 199–217. 2011. DOI 10.1002/bmc.1560.

10. OZAWA, Takeo. Thermal analysis—review and prospect**. Thermochimica Acta**. v. 355, n. 1–2, p. 35–42. 2000.

11. PEREIRA, E.D., SOUZA, F.G., SANTANA, C.I., SOARES, D.Q., LEMOS, A.S. and MENEZES, L.R. Influence of magnetic field on the dissolution profile of cotrimoxazole inserted into poly(lactic acid-co-glycolic acid) and maghemite nanocomposites**. Polymer Engineering & Science**. v. 53, n. 11, p. 2308–2317. 2013. DOI 10.1002/pen.23606.

12. PEREIRA, Emiliane Daher, CERRUTI, Renata, FERNANDES, Edson, PEÑA, Luis, SAEZ, Vivian, PINTO, José Carlos, RAMÓN, José Angel, OLIVEIRA, Geiza Esperandio and SOUZA JR, F.G. Influence of PLGA and PLGA-PEG on the dissolution profile of oxaliplatin**. Polímeros**. v. 26, n. 2, p. 137–143. 2016. DOI 10.1590/0104-1428.2323.

13. FERREIRA, Letícia Pedretti, DA CUNHA, Bruno Pereira, KUSTER, Ricardo Machado, PINTO, José Carlos, SOUZA, Marcio Nele and SOUZA JR., F.G. Synthesis and chemical modification of poly(butylene succinate) with rutin useful to the release of silybin**. Industrial Crops and Products**. v. 97, p. 599–611. 2017. DOI 10.1016/j.indcrop.2016.12.064.

14. FIGUEIREDO, André Segadas, ICART, Luis Peña, MARQUES, Fernanda Davi, FERNANDES, Edson Rodrigo, FERREIRA, Letícia Pedretti, OLIVEIRA, Geiza Esperandio and SOUZA, Fernando Gomes. Extrinsically magnetic poly(butylene succinate): An up-and-coming petroleum cleanup tool**. Science of The Total Environment**. v. 647, p. 88–98. 2019. DOI 10.1016/j.scitotenv.2018.07.421.

15. GRANCE, E. G. O., SOUZA JR., F. G., VARELA, A., PEREIRA, E. D., OLIVEIRA, G. E. and RODRIGUES, C. H. M. New petroleum absorbers based on lignin-CNSL-formol magnetic nanocomposites**. Journal of Applied Polymer Science**. v. 126, n. S1, p. E305–E312. 2012. DOI 10.1002/app.36998. 0000

16. CAETANO, Rosana M.J., BEDOR, Priscilla B.A., DE JESUS, Edgar F.O., LEITE, Selma G.F. and SOUZA JR., F.G. Oil Biodegradation Systems Based on γ Irradiated Poly (Butylene Succinate)**. Macromolecular Symposia**. v. 380, n. 1, p. 1800123. 2018. DOI 10.1002/masy.201800123.

17. FERREIRA, L.P., MOREIRA, Andrei N., DELAZARE, Thaís, OLIVEIRA, Geiza Esperandio and SOUZA JR., F.G. Petroleum Absorbers Based on CNSL, Furfural and Lignin – The Effect of the Chemical Similarity on the Interactions among Petroleum and Bioresins**. Macromolecular Symposia**. v. 319, n. 1, p. 210–221. 2012. DOI 10.1002/masy.201100145. 0000

