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Potentiation of Paracetamol using Mid-infrared Rays

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Abstract

Potentiation of drugs is most needed and an emerging science in the pharmaceutical industry, but meager work has been done. At present potentiation is done by additives/ synergistics but disadvantages are many. In this study, packaged paracetamol tablets were subjected to a mid-infrared (mid-IR) irradiation. The mid-IR was applied through a 2-6 µm mid-IR generating atomizer (MIRGA), recently invented by us. These tablets were clinically trialed and compared with non-irradiated control. The mid-IR exposed tablet dose requirement was reduced by 30-40%which results in the reduction of host stress, overdosing, and cost economical. In summary, clinical trial data and instrumentations validate the mid-IR's favorable effect on paracetamol.

Keywords: MIRGA, 2-6µm mid IR, Paracetamol, Irradiation, Potency Enhancement, Economical.

Introduction

Paracetamol, 147 years aged, most acquired analgesic drug available without prescription. Paracetamol has worldwide common use, safe at recommended dose, but at higher dose cause harmful effect on various systems including foetus [1-3]. Generally, as the years advance, the dose of every allopathic medicine is gradually increasing. Concurrently raising voice against the dose increment, is now getting paramount importance, whereas research on this subject is scarce. In this pioneer research, by applying mid-IR, we potentiated the marketed paracetamol tablets which reduced its clinical dose requirement and thus made safer, less economy and resource saving.

Material and Method

MIRGA (patent no.: 401387) is a 20 ml pocket sized atomizer (Supplementary file – figure F1) containing inorganic water based solution in which approximately two sextillion cations and three sextillion anions are contained. During spraying, depending on pressure (vary with the user) applied to plunger, every spraying generates 2-6µm mid-IR. Design of the MIRGA and emission of 2-6µm mid-IR has been presented in detail by Umakanthanet al., 2022a; Umakanthanet al., 2022b; Umakanthanet al., 2023c; Umakanthanet al., 2023d [4-7]. Every time spraying emits 0.06ml which contains approximately seven quintillion cations and eleven quintillion anions. (details about MIRGA available in supplementary text T1).

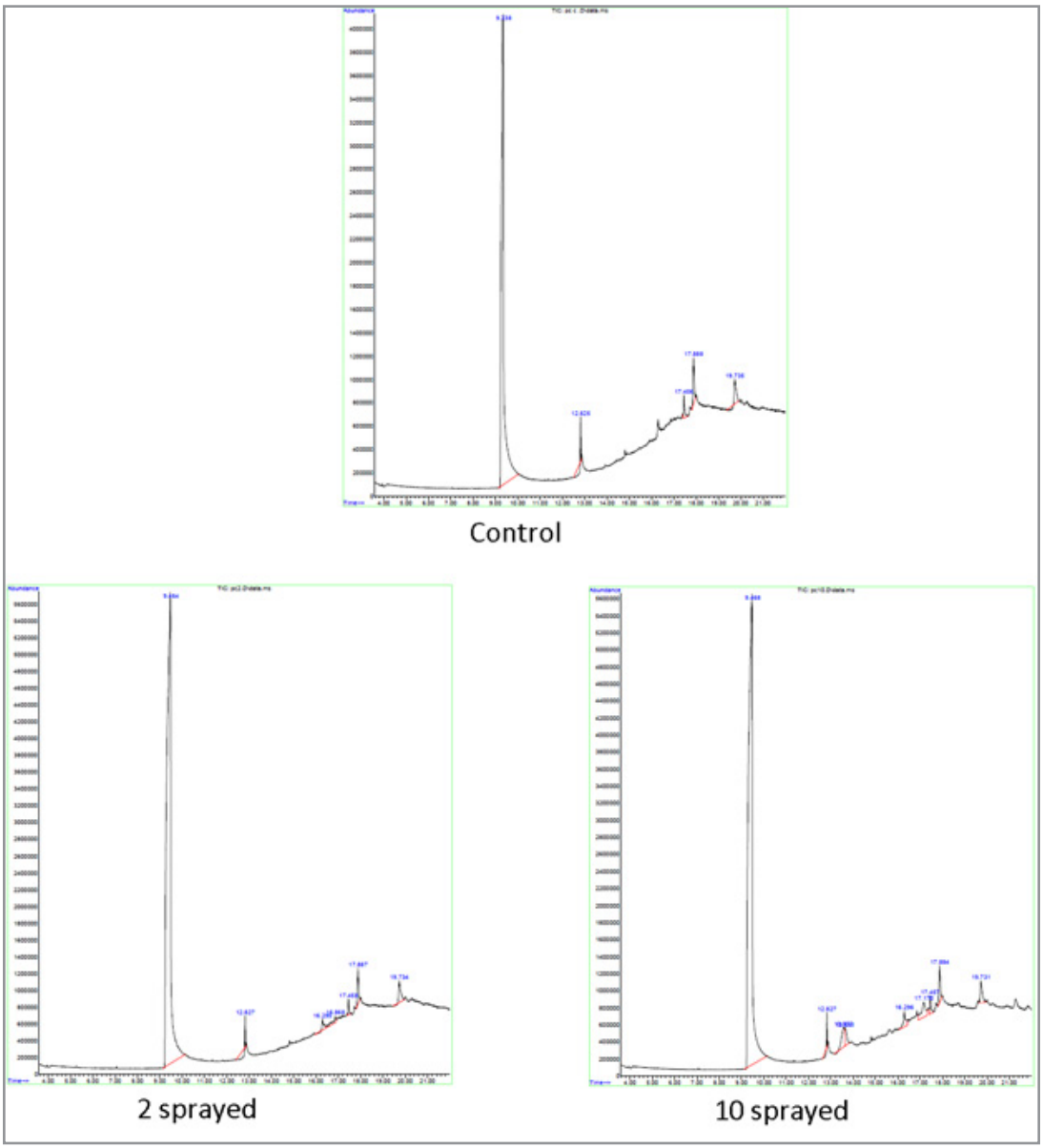


Figure 1: GC-MS spectra of Paracetomol

Marketed strips with paracetamol tablets (500 mg) each containing 10 tablets (polyethene packed) packets were locally purchased and used. Sensory export panel (n:6) service was also used.

The instruments used to demonstrate the irradiation changes in paracetomol are:
Chemical compound transformation – Gas chromatography–mass spectrometry (GC-MS): Agilent technologies, 7820 GC system, 5977E MSD, Column DB-5, Over temp 100-2700C, Detector MS, Flow rate 1.2, Carrier gas Helium.

Chemical bond changes – Transform infrared spectroscopy (FTIR):
JASCO FT-IR 4200 plus spectrophotometer with ATR (range 4000–400 cm^{-1} at 298 K) and IR AFFINITY I – FTIR Spectrophotometer, FTIR 7600, Shimadzu.

Structural changes – Powder X-ray diffraction (PXRD):
XRD Diffractometer (powder) Philips Xpert MPD Range (2θ): 3º to 136º; X-ray tube: Cu; JCPDF database; 2θ vs intensity plots; X-Ray Power: 2KW; Software: JCPDF database for powder diffractometry).

Proton resonances – Proton nuclear magnetic resonance (1H-NMR):
H1 NMR spectra of Paracetomol samples (~8mg for 1H) in "DMSO-D6 (Eurisotop, France)" were acquired using a 300 MHz AVANCE II (Bruker Biospin, Switzerland) spectrometer equipped with a 5mm BBO probe (Bruker BioSpin, Switzerland). The experiments were recorded at 298.15 K using the standard pulse sequence library of TopSpin 3.2 (Bruker Biospin, Switzerland) followed by processing of the data by using TopSpin 3.2 (Bruker Biospin, Switzerland) software.

Configuration – Transmission electron microscopy (TEM):
FEI Technai Spirit G2, HT 120KV, Electron source LaB6, Netherlands.

Contour and signal-to-noise ratio – 3D fluorescence spectroscopy:
3D Fluorescence spectra were measured on a Hitachi F-7000 spectrophotometer in the range of 200-700 nm (fluorescence) at 298 K. The spectral patterns were analyzed using an original software (Hitachi).

The spraying was conducted from a distance of 0.25 to 0.50 meter towards the packaged (polythene) paracetamol tablet strips (Method of MIRGA spraying in Supplementary file – video V1). This distance is very important for the creation of ion clouds, oscillation, and 2-6 µm mid-IR generation during MIRGA spraying. The mid-IR can penetrate the intervening media (polythene package) and act on the paracetamol inside. It should note that close-ranged sprayings do not generate energy. MIRGA is used like a body spray.

Eleven packets (10 tablets x 10 strips) were purchased and used in this study. The first packet was marked as C (Control).The remaining 10 packets were numbered 1-10 and correspondingly exposed 1-10 MIRGA spraying from 0.25–0.50 meter distance externally over the packet. Sensory panel experts from pharmaceutical industry were employed as trained experts. The applied acceptability index was hedonic scale with a 9-point nominal structure 1 - Dislike extremely, 2 - Dislike very much, 3 - Dislike moderately, 4 - Dislike slightly, 5 - Neither like nor dislike, 6 - Like slightly, 7 - Like moderately, 8 - Like very much, 9 - Like extremely [8, 9]. After every spraying, trial samples were tested and clinically used to treat the patients with pyrexia, migraine, and acute and chronic pain. Post therapy history elucidation of the patients showed that the control sample had normal effect, but 2 sprayed had more effect than control, 1 and 3 to 10 sprayed samples. Accordingly, the 2-sprayed paracetamol dose was reduced from routine 500 mg to 250-350 mg. The reduced dose (250-350mg) was then tried in patients. The non-sprayed sample marked C (Control) and potentiated (2-sprayed) and potency reduced (10-sprayed) samples were subjected to the various instrumentations. The results were compared regarding the various parameter changes caused by the mid-IR.

The expert panel could feel the taste difference between 1 and 5 minutes of sprayings. The reason for more spraying (i.e. here 10) is: in nature input of more energy to food/ water/ anything including 5 basic elements denatures their natural characters. Hence, we tried this phenomenon by a greater number of MIRGA spraying to the paracetamol.

Results and Discussion

In 2 sprayed paracetamol mostly 250 mg and in some patient 300-350mg was found to be equally effective as non-sprayed control (500 mg). 10 sprayed paracetamol effect was found to be reduced and hence needed 750-1000 mg for clinical pain relief.

The sensory expert panel opinioned that, compared to control, in 2 and 10 sprayed samples bitterness enhancement and reduction respectively occurred.

Instrumentation Result

(raw data of instrumentations in Supplementary file – Data D1)

Sensory Scores
Table 1 showed that 2 and 10 sprayings respectively had increased or decreased the taste of paracetamol.

Table 1: Sensory scoring of Paracetamol samples

No. of MIRGA sprayings	Sensory scores
Control (non-sprayed	5
1	6
2	8
3	7
4	6
5	6
6	6
7	4
8	3
9	2
10	1

Control, 2 and 10 sprayed paracetamol were subjected to instrumentation. All the samples for a trial were taken from the same source packet, and packets of different batches and brands were not mixed in any trial.

GCMS
Control: The GCMS pattern of this sample shows key peaks at 9.3 min, 12.8 min, 17.4 min, 17.9 min, and 19.7 min.

2 sprayed sample: Compared to the control, sample shows an additional peak at ~16.9 min. The additional peak is attributed to modifications in the formulation that increase the bitterness.

10 sprayed sample: In contrast to the control sample, shows peaks at about 13.6 min, 16.2 min, and 17.1 min. Researchers have reported that the bitter taste of acetaminophen can be inhibited by addition of substances that mask the bitter taste. The additional peaks in the GCMS pattern of this sample are ascribed to possible substances that mask the bitter taste. (Table 2)

Table 2: GCMS analysis of paracetamol

R t (min)	Name of compound	% Area present in each sample			Remarks
		Control	2 sprayed	10 sprayed	
12.82	Acetaminophen (Paracetamol)	91.66	94.20	86.22	
13.60	Possibly octadecadienol	ND	ND	4	Increased upon 10 spraying.
16.29	7-pentadecyne	ND	0.78	1.51	Increased upon 2 spraying. Compound reported as a component from plants with antimicrobial activity.

17.45	Possibly a fatty acid degradation product.	1.79	0.69	1.06	Decreased in sprayed samples.
17.88	9-octadecenal	4.4	2.06	2.18	Decreased in sprayed samples.
14.84	E-9-octadecenoic acid 2,3 dihydroxipropylester	2.5	0.0	0.0	Completely disappeared in sprayed samples.

FTIR

(a) JASCO FT-IR 4200 plus spectrophotometer with ATR (range 4000–400 cm^{-1} at 298 K)

Average Transmission Response in All Samples:
The average transmission signal drops in 2 sprayed samples, but it raises again in 10 sprayed sample. Therefore, the overall absorption by the sprayed samples in the mid-infrared spectrum is a mix and complex behavior depending on the number of spraying.

Control Sample: The spectral features observed at 1850-1900 cm-1, 2800 cm-1, 3320 cm-1, 3200-3600 cm-1, seen amongst others in the functional group region, are respectively associated with the stretching vibrations of C=O, C-H, N-H, O-H in paracetamol [10].

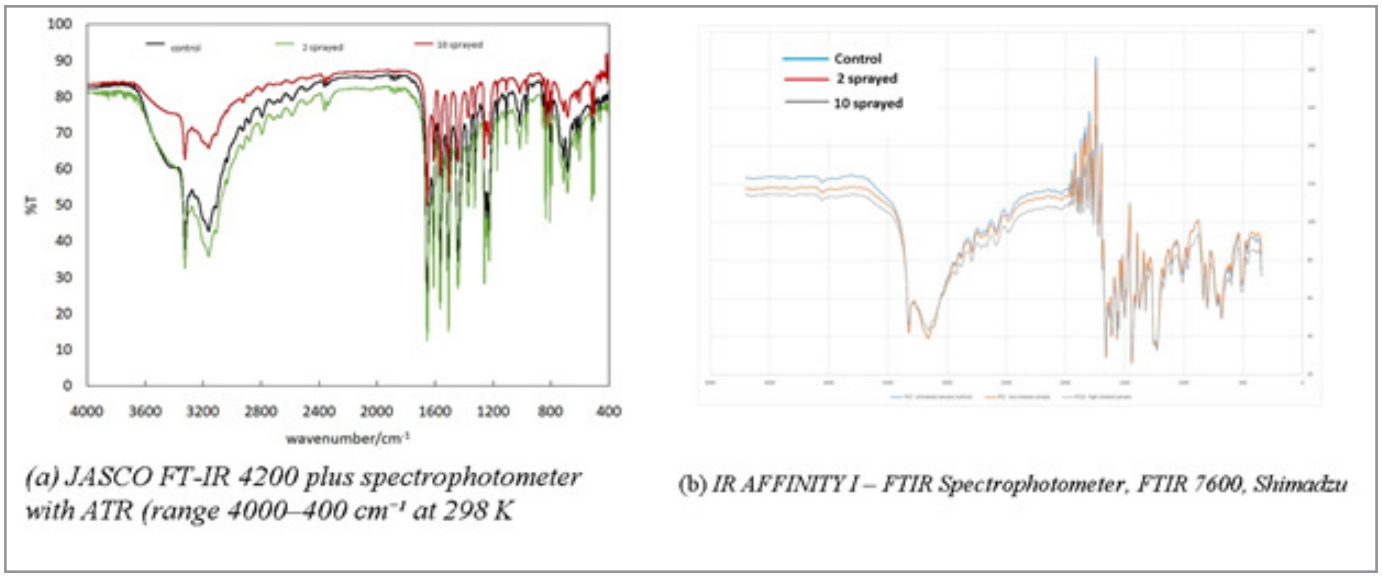
2 sprayed Sample: In the functional group region, in addition to a shift in the background signal, there is a slight increase in most peak signals, especially the N-H bond at 3320 cm-1.

10 sprayed Sample: The peak levels in the fingerprint region reduced significantly, indicating a trend towards structural distortion in this sample. In the functional group region, in addition to the shift in the background signal, the broad C=O pattern in the range of 1850-1900 cm-1 decreased significantly compared to the control and 2 sprayed samples, which is in-line with the distortion trend observed in the fingerprint region. The same behavior can be seen at the peaks associated with the stretching vibrations of C-H, N-H, O-H respectively at 2800 cm-1,3320 cm-1, 3200-3600 cm-1, all of which agree with a structural distortion of this sample.

The observed changes in the stretching vibrations, as well as the distortion effects seen in the 10 sprayed sample, which is interpreted as to the 2 sprayed sample being more favorable than the control sample, and the 10 sprayed sample being less favorable [11]. (Fig 2a)

(b) IR AFFINITY I – FTIR Spectrophotometer, FTIR 7600, Shimadzu

Compared to control, 2 sprayed paracetamol has OH, NH, CO and secondary amide groups which should have caused increased bitterness than control. Benzene ring is not observed in 2 sprayed paracetamol, this could be due to deep decomposition of paracetamol followed by oxidation. 10 sprayed has lower paracetamol concentration than control and as part of flavoring additives, upon observation they were monosaccharides, which have reduced the paracetamol's bitterness. (Fig 2b)



(a) JASCO FT-IR 4200 plus spectrophotometer with ATR (range 4000–400 cm^{-1} at 298 K

(b) IR AFFINITY I – FTIR Spectrophotometer, FTIR 7600, Shimadzu

Figure 2: FTIR spectra of Paracetomol

PXRD

The diffractogram of 2 sprayed and 10 sprayed samples presented a series of intense peaks, which indicates that they are crystalline in nature. The characteristics diffraction peaks are present at 15-degree, 18 degree, 20 degree and 23 degree and 25 degree. However, the control sample shows a broad peak at 25 degree. (Fig 3)

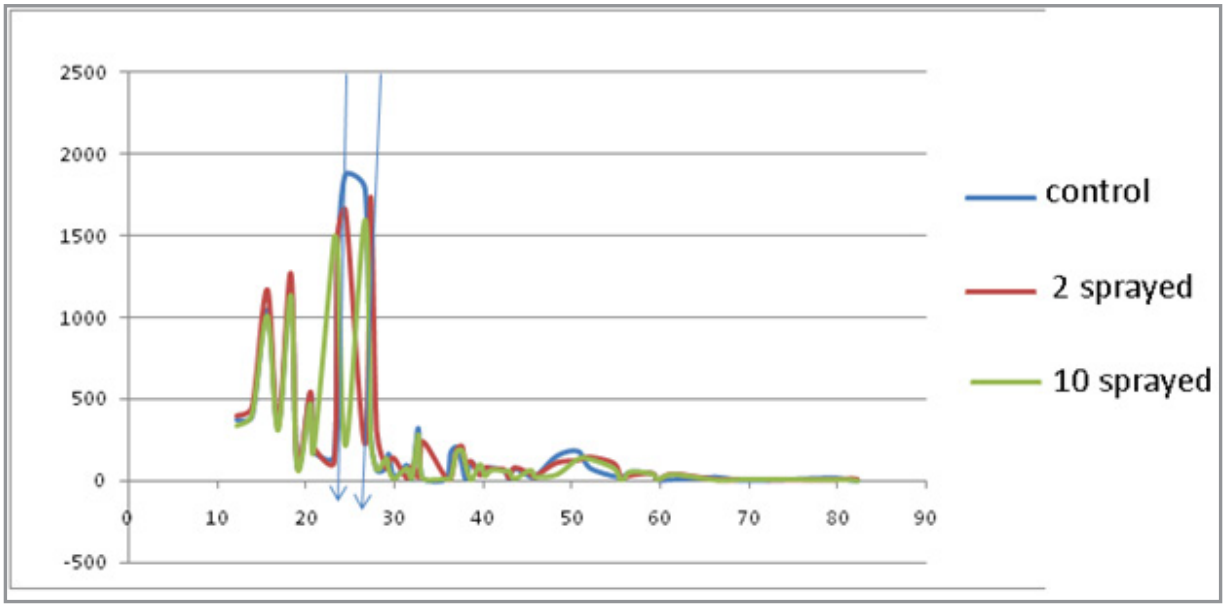


Figure 3: PXRD of Paracetomol

The samples are crystalline in nature. However, in control sample, aggregation is found. 2 sprayed and 10 sprayed samples are not degraded after spraying, and the crystallinity increased.

3D Fluorescence Spectroscopy

Compared to the control and 10 sprayed sample, the fluorescence fingerprint of the 2 sprayed samples show more variation in the contour, indicating the signal–to–noise ratio has been changed. (Fig 4)

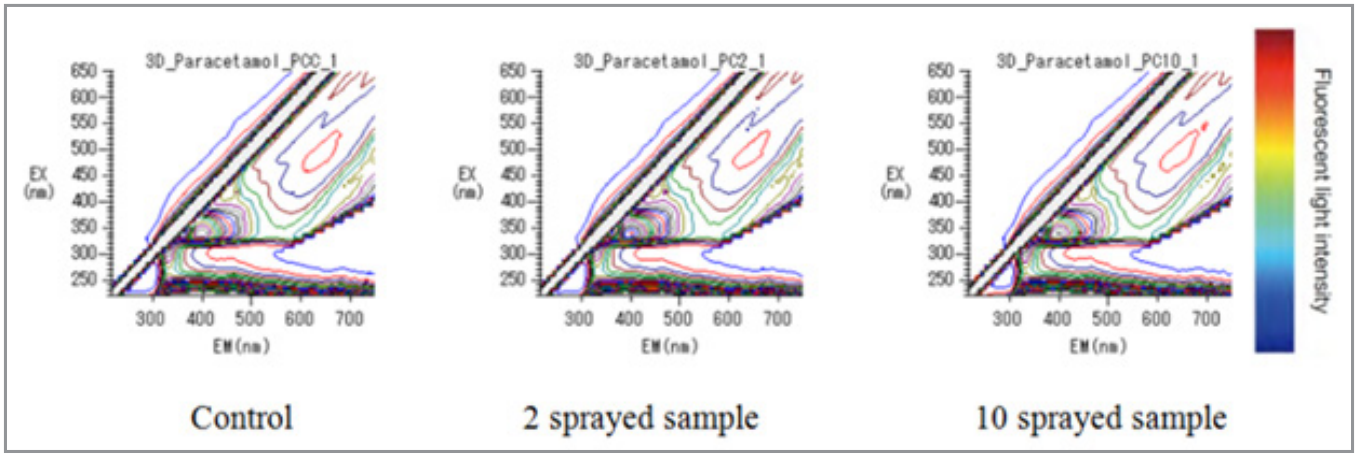


Figure 4: 3D Fluorescence spectra of Paracetamol

Proton NMR

The intensity of peak is very high in 2 times sprayed sample and low in 10 times sprayed sample. Hence decomposition is happening in 10 sprayed sample. In both cases (2 & 10 sprayed) number of protons are the same. But in 10 sprayed sample, the compound decomposed and there is a smaller number of molecules present, hence efficiency decreased. (Fig 5)

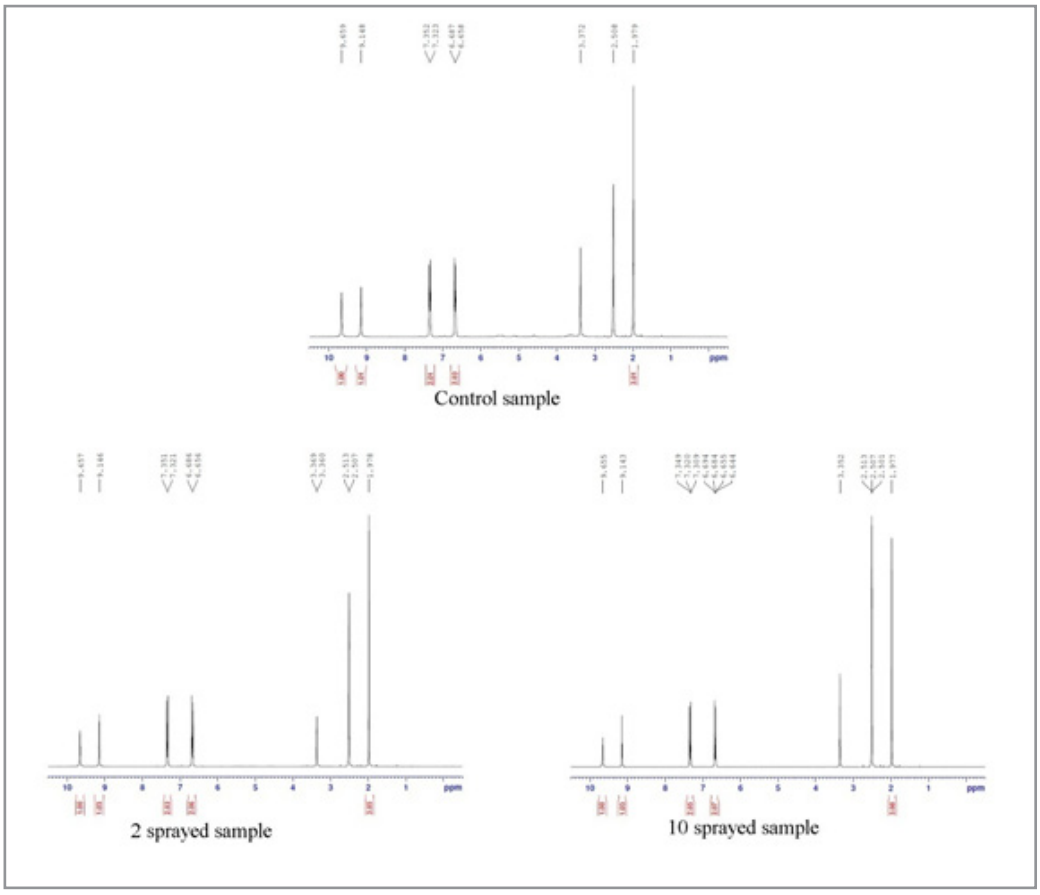


Figure 5: 1H-NMR of Paracetamol

HR-TEM

In control sample, different arrangements of mass distribution within amorphous-shaped aggregates, different types of individual particles in the micrometer size range, and cluster of nanoparticles are observed. Homogeneous aggregates are frequently observed. Aggregates are mostly characterized by a fragmented structure. Also adjacent to aggregates, presence of a chain-like cluster of semi-spherical nanoparticles, roughly sized 60 – 80 nm (diameter) are found. A apparent thickness of nanoparticles is similar to that of the aggregate, suggesting that the cluster is formed by the same material, and mass distribution, of the aggregate itself. Individual particles show sizes in the micrometer range. Apparent thickness and mass distribution within particle body are evidently different: flat and partially folded, multilayer, compact. Differences are correspondingly observed also in edges shape: rounded and squared. Nanoparticles in the cluster have 20 – 30 nm diameter, that is lower than size of nanoparticles in the chain-like cluster.

2 sprayed sample has different arrangements of mass distribution within amorphous-shaped aggregates; in particular shows a more inhomogeneous mass distribution, where needle-like edges are visible. Also, crystal-like particles in the sub micrometer size and nanoparticles cluster are visible. Aggregates observed in the 2 sprayed samples are far more compact, showing quite homogeneous distribution of the mass within aggregate, and a number of dark objects included in the aggregate matrix, either particles, or spots; their sizes range 20 – 50 nm. In the control sample mass arrangement is minorly observed, in the 2 sprayed sample it is frequently observed. In the aggregate a cluster of semi-spherical nanoparticles is observed that appears linked to the aggregate body, similarly that observed in control sample. Also size of clustered nanoparticles is comparable (40 – 60 nm). Main mass distribution is strongly inhomogeneous, with sponge-like aspect, and indented edges; peculiar needle-like fragments are observed, sized 0.5 – 0.8 µm length and ab. 20 nm width. Crystal-like particles are documented which appear square-shaped, with long and short sides respectively sized ab. 300 nm and 100 nm. Nanoparticles diameter ranges 10 – 30 nm.

In 10 sprayed sample both aggregates and nanoparticles structures appear very different. Mass fragments are far more overlapped and closed within a more limited area. Mass distribution appears strongly inhomogeneous suggesting that the material is forced to converge toward some areas. Concerning clusters, particles are in the sub micrometer size and appear strongly overlapped. Size ranges are 0.3 – 0.6 µm for major axis and 0.2 – 0.3 µm for minor axis, considering their ellipsoidal shape. Main differences with respect to control and 2 sprayed samples are in the cluster size and shape: nested clusters are not observed in previous samples, while chain-like clusters appear longer than in the control and 2 sprayed samples. Nevertheless, nanoparticles size remains comparable ranging 10 – 40 nm.

In summary, with respect to the structure of control sample, the responses of 2 sprayed and 10 sprayed samples lead to increasing differences. In particular, in 2 sprayed sample main components of the original matrix are still observed, concerning both aggre-

gates and nanoparticle clusters; however, the abundance of aggregate types is overall inverted (particularly concerning the aggregate including nanosized dark spots, that is minorly observed in the control, and majorly observed instead in the 2 sprayed sample). In the 10 sprayed sample, instead, both aggregates and nanoparticle clusters show evident differences in structure and (concerning aggregates) mass distribution [12]. A common feature of both seems to be the stronger mass aggregation, likely due to the 10 sprayings. This could explain both the observations of materials forced to "converge" toward some areas with respect to others (aggregates), and larger number of nanoparticles grouped by the same cluster (while, instead, nanoparticle sizes remain unchanged). (Fig 6)

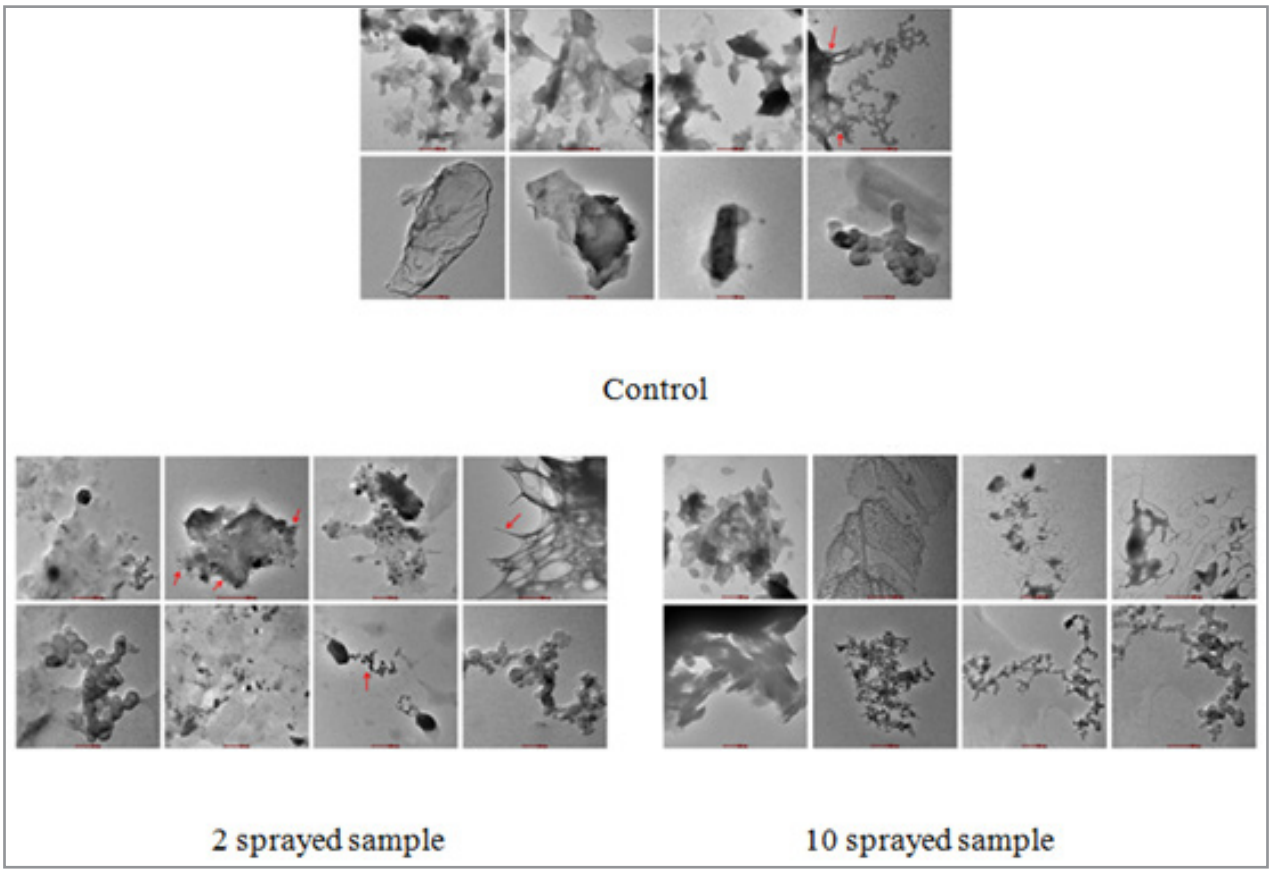


Figure 6: TEM Bright-field images of Paracetamol

Action of mid-IR on Paracetamol

Invention background, definition, technique of mid-IR generation from MIRGA, toxicological study on MIRGA, safety of the MIRGA sprayed usables and primeval and future scope of MIRGA have been described by Umakanthan et al., 2022a and Umakanthan et al., 2023d (detailed discussion on MIRGA available in supplementary text T2) [4, 7].

In the electromagnetic wave (EMW) spectrum mid-IR region is vital and interesting for many applications since that region coincides with the internal vibration of most molecules [13]. Almost all thermal radiation on the earth surface lies in the mid-IR region, 66% of the sun's energy we receive is infrared and is absorbed and radiated by all particles on the earth [14]. Naturally, at molecular level, interaction of mid-IR wavelength energy elicits rotational and vibrational modes (from about 4500-500 cm-1 roughly 2.2 to 20 microns) through a change in dipole movement leading to chemical bond alteration [15].

Paracetamol is a commonly sold medicine without prescription, hence more in use. So there is every chance for many benefits including resource saving by administration of potentiated (sprayed) paracetamol. This MIRGA technology is easy, needs no extra manufacturing/ processing sophistication/ labor cost. MIRGA is highly economical and without adverse effect because mid-IR is biologically safe, although it penetrates most barriers [16]. Mid-IR is easily absorbed by the biomolecules, followed by vibration mode change leading to other process as demonstrated here, viz., changes in N-H bond, C=O pattern, C-H, N-H, O-H stretching, distortion of structure, oxidation, concentration of paracetamol, etc. which are responsible for potency enhancement [17-22]. Also demonstrated is the effect of extra input of 2-6 μm mid-IR energy which caused the potency reduction. This is a better outcome when compared to a recent study that glucosamine (GlcN) was found to increase the bioavailability of paracetamol by reducing its metabolism, leading to higher levels of paracetamol in the body [23].

Reducing the dose of paracetamol may have potential risks and benefits. Some experts believe that therapeutic doses of paracetamol can cause hepatotoxicity, leading to liver damage [24]. However, this view is not supported by much evidence, as paracetamol is generally well tolerated at recommended doses [25]. On the other hand, reducing the dose of paracetamol may help

in reducing the risks of deliberate and accidental overdose [26]. It was felt important to educate caregivers about the potential for toxicity and review dosing guidelines based on age and weight during each visit [27]. However, it is worth noting that paracetamol is still considered a suitable first-line analgesic for mild to moderate acute pain in many adults with various comorbidities [28]. Therefore, the present study using MRIAG to reduce the dose of paracetamol is found necessary at this time in medicinal practice.

The inorganic compounds used in the generation of MIR are a perspective for biomedical applications [29, 30]. It is also a new synthesis method for preparation of functional material (2-6 µm mid-IR) [31, 32]. It is well known that the combination of different compounds, which have excellent electronic properties, leads to new composite materials, which have earned great technological interest in recent years [33, 34].

Similar desirable results in coffee, tea, cocoa, edible salts and terminaliawere achieved using MIRGA spraying by Umakanthanet al., 2022a; Umakanthanet al., 2022b; Umakanthanet al., 2023c; Umakanthanet al., 2023d [4-7].

Conclusion

Paracetomol tablets were irradiated with 2-6 µm mid-IR and clinically tried for its potentiated analgesic effect. This technology has reduced the paracetamol dosage by 30-40% from the usual dose hence economy, resource savings and reduced host stress. The mid-IR wavelength may be tried for potentiation of other medicines, thereby chances of reduction of dosages.

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Author Contribution

- **Umakanthan:** Conceptualization, Methodology, Supervision, Validation.
- **MadhuMathi:** Data curation, Investigation, Visualization, Writing - Original draft preparation.
- **Umadevi:** Project administration, Resources
- **Umakanthan, MadhuMathi:** Writing- Reviewing and Editing.

Competing Interest

In accordance with the journal's policy and our ethical obligation as researchers, we submit that the authors Dr.Umakanthan and Dr.MadhuMathi are the inventors and patentee of Indian patent for MIRGA (granted-patent no.: 401387) which is a major material employed in this study.

Data and Materials Availability

All data is available in the manuscript and supplementary materials.

Supplementary file available in: https://docs.google.com/document/d/1wNartkUXIccQpw-z2BXyP_1YUZrEzW91/edit

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References

1. Andrade S, Martinez C, Walker A (1998) Comparative safety evaluation of non-narcotic analgesics. J Clin Epidemiol 51: 1357-1365.
2. Rutkowski K, Nasser SM, Ewan PW (2012) Paracetamol Hypersensitivity: Clinical Features, Mechanism and Role of Specific IgE. International Archives of Allergy and Immunology 159: 60-64.
3. Ferner RE, Dear JW, Bateman DN (2011) Management of paracetamol poisoning. BMJ 342: d2218.
4. Umakanthan, Mathi M (2022) Decaffeination and improvement of taste, flavor and health safety of coffee and tea using mid-infrared wavelength rays. Heliyon 342: d2218.
5. Umakanthan T, Mathi M (2022) Quantitative reduction of heavy metals and caffeine in cocoa using mid-infrared spectrum irradiation. Journal of the Indian Chemical Society 100: 100861.
6. Umakanthan T, Athi M (2023) Increasing saltiness of salts (NaCl) using mid-infrared radiation to reduce the health hazards. Food Science & Nutrition 11: 3535-3549.
7. Umakanthan, MadhuMathi (2023) Potentiation of Siddha medicine using Muppu (Universal Potentiator). International Journal of Pharmaceutical Research and Applications 8: 2070-2084.
8. Everitt M (2009) Consumer-Targeted Sensory Quality. Global Issues in Food Science and Technology 117-128.
9. Wichchukit S, O'Mahony M (2014) The 9-point hedonic scale and hedonic ranking in food science: some reappraisals and alternatives. Journal of the Science of Food and Agriculture 95: 2167–2178.
10. Socrates G (2004) Infrared and Raman Characteristic Group Frequencies: Tables and Charts, 3rd Edition. Chichester England John Wiley & Sons Ltd. doi: https://doi.org/10.1002/jrs.1238.

11. Agarwal CM, Joo L Ong, Mark R Appleford, Gopinath Mani (2014) Introduction to Biomaterials: Basic Theory with Engineering Applications. Cambridge university press, UK 81.
12. Atkins P, Juliode Paula (2011) Physical Chemistry for the Life Sciences. Oxford university press Oxford 365.
13. CORDIS, European commission (2019) New advances in mid-infrared laser technology. Compact, high-energy, and wavelength-diverse coherent mid-infrared source. https://cordis.europa.eu/project/rcn/99977/brief/en.
14. Aboud S, Altemimi A, Al-Hilphy A, Lee YC, Cacciola F (2019) A Comprehensive Review on Infrared Heating Applications in Food Processing. Molecules 24: 4125.
15. Girard JE (2014) Principles of Environmental Chemistry. 3rd edition, Jones & Bartlett Learning, USA 99.
16. Pereira MF, Oleksiy Shulika (2011) Terahertz and Mid Infrared Radiation: Generation, Detection and Applications. Springer Science + Business Media B V, The Netherlands. DOI:10.1007/978-94-007-0769-6.
17. Sommer A, Dan Zhu, Adam Mester, Horst-Dieter Försterling (2011) Pulsed Laser Light Forces Cancer Cells to Absorb Anticancer Drugs - The Role of Water in Nanomedicine. Artificial Cells, Blood Substitutes, and Immobilization Biotechnology 39: 169-73.
18. Jung D, Bank S, Lee M L, Wasserman D (2017) Next-generation mid-infrared sources. Journal of Optics 19: 123001.
19. Titterton DH (2015) Military Laser Technology and Systems, Artech House, Boston, London 389. https://books.google.co.in/books?id=UKwxBwAAQBAJ&pg=PA389&dq=mid+wave+infrared+spectrum+bond+vibration&hl=en&sa=X&ved=0ahUKEwjFi_K1v7feAhUEbo8KHXdDAgk4ChDoAQgoMAA#v=onepage&q=mid%20wave%20infrared%20spectrum%20bond%20vibration&f=false
20. Tsai SR, Hamblin MR (2017) Biological effects and medical applications of infrared radiation. J Photochem Photobiol B 170: 197–207.
21. Xu R, Yan Xu (2017) Modern Inorganic Synthetic Chemistry. 2nd end. Elsevier B.V, Netherlands, UK, USA 124.
22. Esmaeili K (2015) Viremedy Homeopathic Remedies, and Energy Healing Remedies as Information – including Remedies; A Synopsis [Revision Aug 2015; E-pub.: Aug.2015] (First Pub: 2013). Google books 43.
23. Joanna G, Anna Olejnik, Aleksander Ejsmont, Aleksandra Galarda, Stefan Wuttke (2021) Overcoming the paracetamol dose challenge with wrinkled mesoporous carbon spheres. Journal of Colloid and Interface Science 586: 673-682.
24. John S, Alchin. Arti, Dhar Kamran, Siddiqui Paul, Christo J (2022) Why paracetamol (acetaminophen) is a suitable first choice for treating mild to moderate acute pain in adults with liver, kidney or cardiovascular disease, gastrointestinal disorders, asthma, or who are older. Current Medical Research and Opinion 38: 811-825.
25. Shilpa S, Thiagarajan Praba, Koyalmannam R, Sethuraman (2019) Paracetamol: The Double-edged Sword Available over the Counter. J Basic Clin Appl Health Sci 2: 79-80.
26. Usama B, Ghaffar Naser, Ashraf Tadvi (2014) Paracetamol Toxicity: A Review. Journal of Contemporary Medicine and Dentistry 2: 12-15.
27. Garry G Graham, Richard O Day, Andis Graudins, Anthoulla Mohamudally (2010) FDA proposals to limit the hepatotoxicity of paracetamol (acetaminophen): are they reasonable? Inflammopharmacology 18: 47-55.
28. Mark G (2015) Research roundup: April 2015. Nurse Prescribing 13: 166-167.
29. Tishkevich DI, Korolkov IV, Kozlovskiy AL, Anisovich M, Vinnik DA, et al. (2019) Immobilization of boron-rich compound on Fe3O4 nanoparticles: Stability and cytotoxicity. J Alloys Compd 797: 573-581.
30. Dukenbayev K, Korolkov IV, Tishkevich DI, Kozlovskiy AL, Trukhanov SV, et al. (2019) Fe3O4 nanoparticles for complex targeted delivery and boron neutron capture therapy. Nanomaterials 9: 494.
31. KozlovskiyA L, Alina A, Zdorovets MV (2021) Study of the effect of ion irradiation on increasing the photocatalytic activity of WO3 microparticles. J Mater Sci Mater Electron 32: 3863-3877.
32. El-Shater RE, Shimy HE, Saafan SA, Darwish MA, Zhou D, et al. (2022) Synthesis, characterization, and magnetic properties of Mnnanoferrites, J Alloys Compd 928: 166954.
33. Kozlovskiy AL, Zdorovets MV (2021) Effect of doping of Ce4+/3+ on optical, strength and shielding properties of (0.5-x) TeO2-0.25MoO-0.25Bi2O3-xCeO2 glasses. Mater Chem Phys 263: 124444.
34. Almessiere MA, Algarou NA, Slimani Y, Sadaqat A, Baykal A, et al. (2022) Investigation of exchange coupling and microwave properties of hard/soft (SrNi0.02Zr0.01Fe11.96O19)/(CoFe2O4) x nanocomposites. Mat Today Nano Materials Today Nano 18: 100186.