

Comparative Evaluation of Paracetamol Tablet Formulations from Different Manufacturers in the Libyan Pharmaceutical Market Using Fourier-Transform Infrared (FTIR) Spectroscopy

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تقييم مقارنة لتركيبات أقراص الباراسيتامول من شركات مصنعة مختلفة في سوق الأدوية الليبية باستخدام تقنية مطيافية الأشعة تحت الحمراء (FTIR)

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Abstract:

Paracetamol (N-acetyl-p-aminophenol) is one of the most widely used over-the-counter analgesic and antipyretic medications globally. To ensure quality control, therapeutic efficacy, and detect potential counterfeiting, rigorous analytical evaluation of commercial formulations from various global manufacturing sites is critical. This study employs Fourier-Transform Infrared (FTIR) spectroscopy to perform a comparative evaluation of the chemical integrity and structural equivalence of standard Paracetamol (C₈H₉NO₂) against three commercial Panadol 500 mg formulations manufactured by Bristol Laboratories (United Kingdom) and GSK (Tunisia and Ireland plants). The results demonstrate high structural correlation with matching scores ranging from 93.7% to 95.6% relative to the reference standard. Spectral analysis confirmed characteristic functional groups, including amide carbonyl stretches, aromatic ring vibrations, and hydroxyl/amine stretching zones, corroborating that all sampled manufacturers meet stringent chemical identity requirements.

Keywords: Paracetamol (Acetaminophen), FTIR Spectroscopy (Fourier-Transform Infrared), Functional Group Analysis.

الملخص

يُعد الباراسيتامول (إن-أسيتيل-بي-أمينوفينول) واحداً من أكثر أدوية تسكين الآلام وخفض الحرارة استخداماً على نطاق واسع ودون وصفة طبية على مستوى العالم. ولضمان مراقبة الجودة، والفعالية العلاجية، والكشف عن حالات التزييف المحتملة، يُعد التقييم التحليلي الدقيق للمستحضرات التجارية الواردة من مواقع التصنيع العالمية المختلفة أمراً بالغ الأهمية. تستخدم هذه الدراسة مطيافية الأشعة تحت الحمراء بتحويل فورييه (FTIR) لإجراء تقييم مقارنة للأهمية الهيكلية للباراسيتامول القياسي (C₈H₉NO₂) مقابل ثلاث تركيبات تجارية من بنادول 500 ملغ المصنعة بواسطة مختبرات بريستول (المملكة المتحدة) ومصانع شركة جلاكسو سميث كلاين (GSK) في تونس وأيرلندا.

وتُظهر النتائج ارتباطاً هيكلياً عالياً بنسب تطابق تتراوح بين 93.7% و 95.6% مقارنة بالمعيار المرجعي. كما أكد التحليل الطيفي وجود المجموعات الوظيفية المميزة، بما في ذلك امتدادات كربونيل الأميد، واهتزازات الحلقة العطرية، ونطاقات امتداد الهيدروكسيل/الأمين، مما يؤكد أن جميع الجهات المصنعة للعينات تلبّي متطلبات الهوية الكيميائية الصارمة.

الكلمات المفتاحية: باراسيتمول، مطيافية الأشعة تحت الحمراء بتحويل فورييه (FTIR)، تحليل المجموعات الوظيفية.

1. Introduction

Paracetamol (acetaminophen, N-(4-hydroxyphenyl)acetamide) is a go-to medication for managing mild-to-moderate pain—whether it's a headache, toothache, or joint pain—as well as bringing down fevers. Because people take it in massive quantities all over the world, the market is flooded with generic and brand-name versions made in all sorts of different places. Even though active pharmaceutical ingredients (APIs) have to follow strict international rules, things like how the tablets are manufactured, whether they form different crystal structures (like monoclinic Form I or orthorhombic Form II), and what inactive fillers are added can subtly change how the final product looks on a spectrum [1].

1.1 Structural and Chemical Profile of Paracetamol

From a structural perspective, the paracetamol molecule ($C_8H_9NO_2$, with a molecular weight of 151.16 g/mol) is characterized by a benzene ring substituted at the *para* position by a hydroxyl group (-OH) and a secondary amide group (-NH-CO-CH₃). This unique layout gives rise to active hydrogen-bonding donor and acceptor sites across its crystalline lattice. The presence of both the phenolic hydroxyl group and the acetamide side chain dictates its vibrational behavior, resulting in distinct infrared absorption bands that make it exceptionally well-suited for spectroscopic identification and structural quality control.

When factories make paracetamol tablets, it can actually be a bit tricky because the powder doesn't always compress easily and tends to cap or break apart during direct compression. To get around this, big manufacturers like Bristol Laboratories and GlaxoSmithKline (GSK) use wet or dry granulation methods, mixing in things like maize starch, microcrystalline cellulose, povidone, and magnesium stearate. These extra ingredients are completely necessary to help the pill hold together and dissolve properly in your stomach, but they also introduce extra chemical signatures that can overlap with or slightly shift the signals you want to see [1].

That's where Fourier-Transform Infrared (FTIR) spectroscopy comes in handy; it's a fast, non-destructive way to fingerprint organic compounds right inside a finished pill [2]. While traditional methods like HPLC are great for measuring exact amounts, they take a lot of time, require messy extraction solvents, and involve a ton of prep work. FTIR lets us skip the chemistry lab solvents and look right at the active ingredients and background materials using simple correlation math [3].

Building on existing screening techniques, this study takes a clean, certified paracetamol reference standard and compares it head-to-head with three commercial "Panadol" 500 mg tablets from different Bristol and GSK plants. The goal is simply to see how well they match up and whether manufacturing differences or regional fillers change the final quality profile.

2. Materials and Methods

2.1 Materials and Reagents

The baseline control used for this study was a certified pure Paracetamol chemical reference standard ($C_8H_9NO_2$, Batch: Std Paracetamol-09 12350). To see how different locations stack up, we grabbed three lots of 500 mg over-the-counter tablets from verified supply chains:

- **Sample No. 1:** Panadol 500 mg, made by **Bristol Laboratories Ltd.** (United Kingdom); Batch Identifier: M322020.
- **Sample No. 2:** Panadol 500 mg, made by **GSK** (Tunisia plant); Batch Identifier: 132925.
- **Sample No. 3:** Panadol Advanced 500 mg, made by **GSK** (Ireland plant); Batch Identifier: RMBM.

2.2 Sample Preparation and Spectral Acquisition

To obtain representative and consistent samples, five tablets were randomly selected from each batch. The tablets were first weighed to assess their weight uniformity and then finely powdered using an agate mortar and pestle. Grinding the tablets into a homogeneous powder helped minimize variations caused by differences in tablet composition, coating, or distribution of the active ingredient [4].

The powdered samples were analyzed using a calibrated Fourier-transform infrared (FTIR) spectrophotometer over the mid-infrared region from 4000 to 500 cm^{-1} . Prior to each measurement, a background spectrum was recorded automatically to account for and minimize interference from atmospheric components, particularly moisture and carbon dioxide. The instrument was operated at a spectral resolution of 4 cm^{-1} , and 32 scans were

collected and averaged for each sample. This approach improved the signal-to-noise ratio and produced clearer and more reproducible spectra.

For analysis, a small amount of each powdered sample was placed evenly on the sampling crystal, ensuring good and consistent contact with the crystal surface. The resulting spectra were recorded as percentage transmittance (%T) as a function of wavenumber. The obtained spectra were then used to identify the characteristic absorption bands of paracetamol and to compare the commercial formulations with the reference standard.

2.3 Chemometric and Data Processing

Following spectral acquisition, the FTIR data were analyzed using the instrument's spectral matching software and an established infrared reference library [2]. Each commercial paracetamol sample was compared with the spectrum obtained from the pure paracetamol reference standard.

The software generated a matching score (%), which represents the degree of similarity between the sample spectrum and the reference spectrum. The comparison was based on the overall spectral profile, including the position, intensity, and shape of the characteristic absorption bands [3]. Higher matching scores therefore indicated greater spectral similarity between the commercial formulation and the pure paracetamol standard.

3. Results and Discussion

3.1 Peak Assignment and Vibrational Interpretation

The FTIR spectrum obtained for the pure paracetamol reference standard showed the characteristic absorption bands expected from its molecular structure. These bands were assigned to the major functional groups and vibrational modes of paracetamol and were subsequently used as reference points for evaluating the commercial formulations [4].

A broad and prominent absorption band was observed at 3325.2 cm^{-1} , corresponding mainly to the stretching vibrations of the phenolic O–H and amide N–H groups. The broad nature of this band can be attributed to hydrogen bonding between molecules in the solid state, which is typical of paracetamol [5].

The strong absorption band at 1654.92 cm^{-1} was assigned to the amide I band, which is primarily associated with the C=O stretching vibration of the acetamide group. This band represents one of the important characteristic features of the paracetamol spectrum [4].

Several distinct absorption bands were also observed at 1612.49 , 1562.34 , and 1504.48 cm^{-1} . These bands are associated mainly with skeletal stretching vibrations of the aromatic ring, particularly C=C stretching. Their presence provides evidence for the characteristic benzene-ring structure of paracetamol [4].

In the region between 1438.90 and 1369.46 cm^{-1} , the observed bands were attributed to bending or deformation vibrations of the methyl ($-\text{CH}_3$) group. These include both asymmetric and symmetric methyl deformation modes and contribute to the characteristic fingerprint of paracetamol [4].

The absorption band at 1226.73 cm^{-1} was assigned to the stretching vibration of the phenolic C–O bond. This relatively strong band is another important feature associated with the phenolic group of the paracetamol molecule [4].

Finally, the absorption observed at 837.11 cm^{-1} was attributed to aromatic C–H out-of-plane bending. This band is particularly useful for confirming the substitution pattern of the benzene ring and is consistent with the para-disubstituted aromatic structure of paracetamol [4].

Overall, the presence and positions of these characteristic absorption bands provided a clear FTIR fingerprint for the pure paracetamol standard. This reference spectrum was subsequently used for comparison with the spectra obtained from the different commercial formulations available in the Libyan market Table 1.

Table 1. Characteristic FTIR Absorption Bands and Vibrational Assignments of the Pure Paracetamol Reference Standard:

Peak Position (cm^{-1})	Assigned Vibrational Mode	Structural Functional Group
3325.20	Phenolic O-H stretch / Amide N-H stretch [5]	Hydroxyl (-OH) & Secondary Amide (-NH-)
1654.92	C=O Stretch (Amide I band) [4]	Carbonyl (C=O)

1612.49, 1562.34, 1504.48	Aromatic ring C=C stretching [4]	Benzene Skeleton (C=C)
1438.90, 1369.46	Methyl group C-H bending modes [4]	Alkyl Methyl (-CH ₃)
1226.73	Phenolic C-O stretching [4]	Aryl Ether / Phenol (C-O)
837.11	Para-disubstituted benzene ring bending [4]	Para-Substituted Aromatic C-H

3.2 Infrared Spectral Profiles and Visualizations

The practical IR spectral signatures, baseline comparisons, and detailed functional overlays captured during the analytical run are displayed below:

- **Figure 1:** Primary Overlaid FTIR Spectral Signatures and Baseline Region Comparison
- **Figure 2:** Detailed Fingerprint Region and Functional Peak Resolution Overlays

3.3 Comparative Spectra Evaluation

When analyzing the IR spectra across the entire frequency range from the active functional group region (4000 - 1500 cm^{-1}) down to the complex fingerprint region (1500 - 500 cm^{-1}) the spectral overlap confirms strong batch consistency [3].

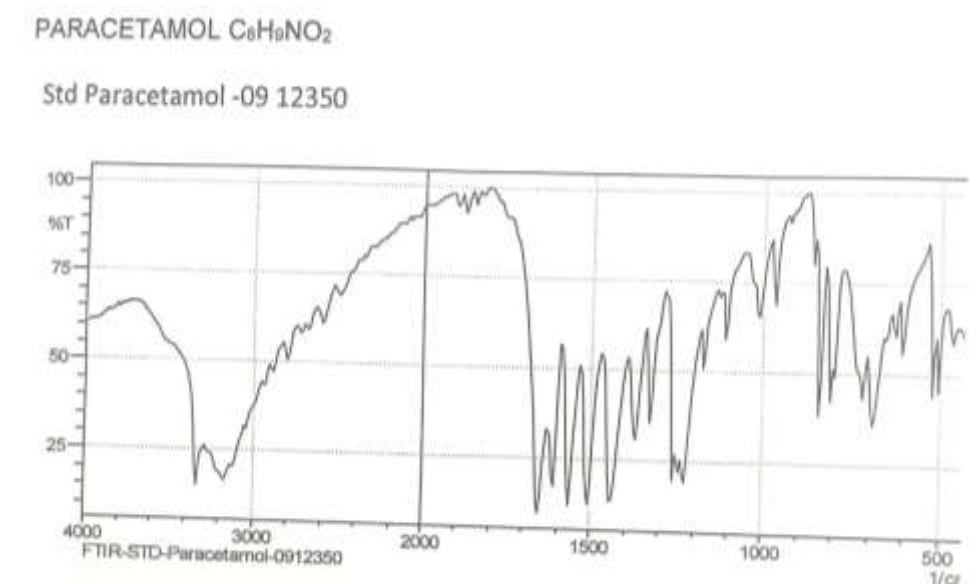


Figure 1. The FTIR spectrum for the standard Paracetamol.

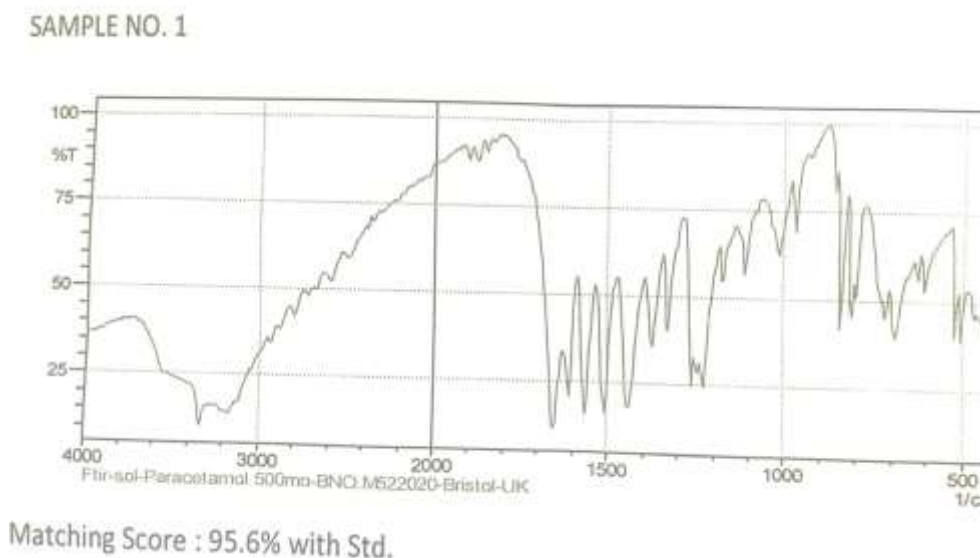
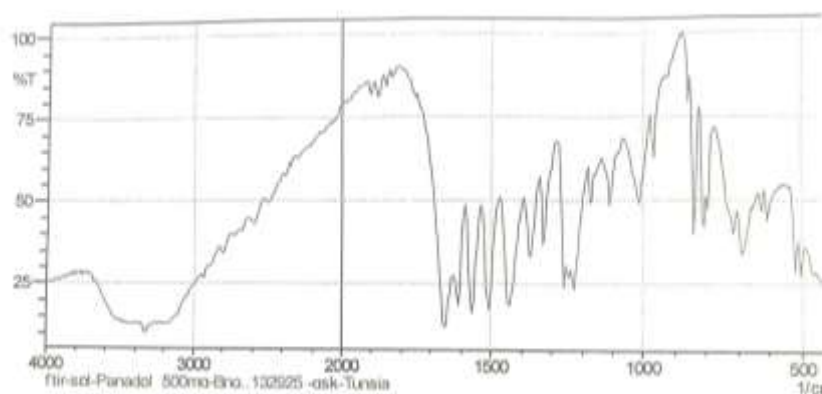


Figure 2. The FTIR spectrum for sample No. 1.

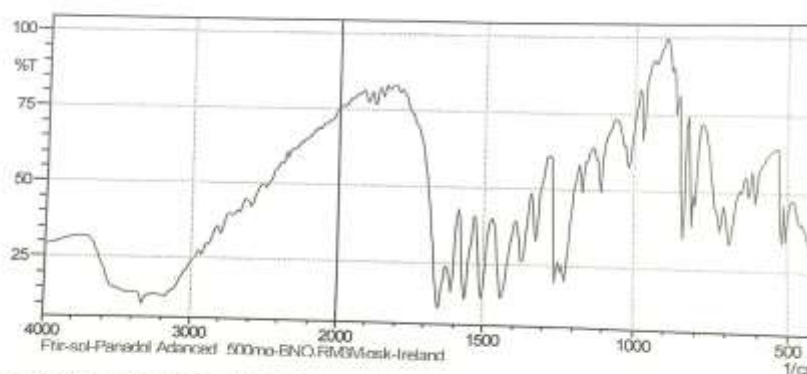
SAMPLE NO. 2



Matching Score : 93.7% with Std.

Figure 3. The FTIR spectrum for sample No. 2.

SAMPLE NO.3



Matching Score : 94.4% with Std.

Figure 4. The FTIR spectrum for sample No.3

As shown in Figures 2, 3, and 4, all three commercial paracetamol formulations exhibited IR spectra that were highly comparable to the reference paracetamol standard (Figure 1). The main characteristic absorption bands of paracetamol were present in all samples, indicating that the active pharmaceutical ingredient (API) was consistent with the reference material.

Sample No. 1, manufactured by Bristol Laboratories (UK), showed the highest spectral similarity, with a match score of 95.6%. The spectrum displayed clear and well-defined absorption bands, particularly within the fingerprint region (1000–600 cm^{-1}). The relatively good spectral resolution and stable baseline suggest that the excipients present in this formulation had little effect on the characteristic spectral pattern of paracetamol [2].

Sample No. 2, manufactured by GSK (Tunisia), produced a match score of 93.7%. The spectrum was also highly similar to that of the reference standard, although some minor baseline differences were observed, particularly in the higher-wavenumber region (3000 – 2000 cm^{-1}). These small variations may be related to differences in sample preparation, contact pressure during ATR measurement, or environmental factors such as moisture. Importantly, these variations did not significantly affect the characteristic absorption pattern of paracetamol [3].

Sample No. 3, manufactured by GSK (Ireland), showed a match score of 94.4%, indicating a high degree of similarity with the reference standard. Although commercial tablet formulations may contain different excipients to improve properties such as tablet disintegration and dissolution, the major IR absorption bands associated with paracetamol remained clearly identifiable. This suggests that the presence of these formulation components did not produce significant changes in the chemical structure of the active ingredient [1].

Overall, the match scores for the three samples ranged from 93.7% to 95.6%, demonstrating a high degree of spectral similarity among the commercial formulations and the reference standard. The relatively small differences in match scores are more likely to be associated with variations in excipient composition, sample preparation, physical characteristics of the tablets, and instrumental or environmental effects rather than chemical degradation of paracetamol. Excipients such as microcrystalline cellulose and maize starch can contribute to minor differences in the overall spectrum, particularly in regions where their characteristic absorptions overlap with weaker paracetamol bands [1].

Therefore, the FTIR results indicate that the three commercial formulations contain paracetamol with a spectral profile closely corresponding to the reference standard. No major spectral differences were observed that would suggest substantial chemical alteration of the active pharmaceutical ingredient. However, FTIR matching primarily provides information about chemical identity and spectral similarity; additional analytical tests would be required to make definitive conclusions regarding drug content, purity, dissolution, or overall pharmaceutical quality.

4. Conclusion

This study confirms that FTIR spectroscopy provides a rapid, reliable, and non-destructive approach for verifying pharmaceutical equivalency across international manufacturing sites [2, 3]. Direct IR spectral evaluation of Panadol 500 mg tablets from Bristol Laboratories and GSK facilities in Tunisia and Ireland proved high chemical conformity with pure paracetamol [1, 4]. With all commercial samples achieving match scores exceeding 93%, the results demonstrate that regional manufacturing processes and local excipient formulations do not compromise the structural integrity of the active pharmaceutical ingredient [1].

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