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Fecal Calprotectin: Beyond a Biomarker of Intestinal Inflammation

From Diagnostic Tool to a Link Between Gut, Immunity, and Systemic Disease

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Abstract

Background.
Fecal calprotectin (FC), a neutrophil-derived S100A8/S100A9 heterodimer, is a widely used non-invasive biomarker of intestinal inflammation, particularly in inflammatory bowel diseases (IBD). Emerging evidence suggests its broader role in gut barrier dysfunction and systemic inflammation.

Aim.
To evaluate the clinical relevance of fecal calprotectin, focusing on its diagnostic performance, limitations, and emerging applications beyond IBD.

Material and methods.

A narrative review of PubMed-indexed literature was conducted, including original studies and reviews addressing the biological role of calprotectin, its diagnostic accuracy, and its association with intestinal permeability, microbiota, and metabolic inflammation.

Results.
Fecal calprotectin demonstrates high sensitivity for detecting intestinal inflammation and is useful in differentiating IBD from functional disorders such as irritable bowel syndrome. Its levels correlate with disease activity and are valuable in monitoring treatment response and predicting relapse. However, its specificity is limited, as elevated levels may occur in infections, malignancies, and drug-related mucosal injury. Recent studies suggest associations between FC, gut microbiota alterations, and low-grade systemic inflammation.

Conclusions.
Fecal calprotectin is a valuable tool in the diagnosis and management of intestinal inflammation. Its expanding role in systemic conditions highlights the need for further research to improve standardization and clarify its clinical applications.

Key words:

fecal calprotectin; intestinal inflammation; inflammatory bowel disease; gut microbiota; intestinal permeability; biomarkers

Introduction

The gastrointestinal tract is increasingly recognized as a central organ in the regulation of systemic homeostasis, extending far beyond its classical digestive functions. It serves as a complex interface integrating immune responses, microbial interactions, and metabolic processes, with the gut microbiota playing a crucial role in shaping both local and systemic immunity [2,19,22]. Disruption of intestinal homeostasis has been implicated not only in primary gastrointestinal diseases but also in systemic inflammatory and metabolic disorders, highlighting the need for reliable biomarkers reflecting intestinal inflammation and barrier dysfunction.

Among the available biomarkers, fecal calprotectin (FC) has emerged as one of the most widely studied and clinically useful non-invasive indicators of intestinal inflammation. Calprotectin is a calcium- and zinc-binding heterodimer composed of S100A8 and S100A9 proteins, predominantly expressed in neutrophils [1,14]. During inflammatory processes, neutrophils migrate into the intestinal lumen and release calprotectin, which can then be detected in stool samples, providing a direct reflection of mucosal inflammation [21]. Importantly, due to its resistance to enzymatic degradation and stability in feces, FC represents a practical and reliable marker suitable for routine clinical use.

The clinical relevance of fecal calprotectin has been most extensively validated in inflammatory bowel diseases (IBD), including Crohn's disease and ulcerative colitis, which are characterized by dysregulated immune responses within the intestinal mucosa [7,26]. Although endoscopy remains the gold standard for assessing disease activity, its invasive nature limits its frequent use. In contrast, fecal calprotectin has been shown to correlate strongly with endoscopic and histological findings, allowing for non-invasive monitoring of disease activity, assessment of treatment response, and prediction of relapse [16,27,29]. This has led to its widespread incorporation into clinical algorithms for the management of IBD.

One of the most important clinical applications of fecal calprotectin is its ability to differentiate between organic inflammatory conditions and functional gastrointestinal disorders. Irritable bowel syndrome (IBS), which is not associated with mucosal inflammation, often presents with symptoms similar to those of IBD. Studies have demonstrated that patients with IBS typically exhibit normal or only mildly elevated FC levels, whereas significantly increased concentrations are indicative of organic pathology, thereby supporting its role as a screening tool in clinical practice [9,12,25].

Despite its well-established utility, fecal calprotectin is not a disease-specific marker, and its interpretation requires careful consideration of clinical context. Elevated FC levels have been reported in a variety of conditions, including gastrointestinal infections, colorectal cancer, necrotizing enterocolitis, and inflammatory states associated with systemic diseases [23,35]. Additionally, factors such as the use of non-steroidal anti-inflammatory drugs and variability in measurement techniques may influence FC levels, further complicating interpretation in clinical settings [3,11].

In recent years, increasing attention has been directed toward the broader role of fecal calprotectin as a marker of intestinal barrier dysfunction and low-grade inflammation. The intestinal barrier is essential for maintaining immune tolerance and preventing the translocation of luminal antigens and microbial products into the systemic circulation. Disruption of this barrier, often referred to as increased intestinal permeability, has been associated with chronic inflammatory states. Neutrophil activation and epithelial responses, in which calprotectin plays an active biological role, may contribute to these processes [6,10].

The interaction between gut microbiota and host immune responses represents another important dimension in the interpretation of fecal calprotectin. The composition and diversity of intestinal microbiota influence immune regulation, epithelial integrity, and metabolic pathways. Dysbiosis has been linked to both inflammatory bowel diseases and metabolic disorders, and several studies have demonstrated associations between altered microbiota profiles and increased fecal calprotectin levels, suggesting that FC may serve as an indirect marker of microbiota-driven inflammation [2,19,22].

Furthermore, emerging evidence indicates that fecal calprotectin may have relevance beyond classical gastrointestinal diseases. Elevated levels have been observed in systemic conditions, supporting the concept that intestinal inflammation may contribute to extraintestinal pathology. This is consistent with the growing recognition of the gut as a key contributor to chronic low-grade inflammation involved in metabolic diseases and other systemic disorders [6,20,34].

Another important aspect of fecal calprotectin is its utility in monitoring disease progression and therapeutic outcomes. Serial measurements have been shown to reflect changes in disease activity over time, enabling early detection of relapse and evaluation of treatment efficacy. This is particularly relevant in IBD, where timely therapeutic adjustments can improve clinical outcomes and reduce complications. As a result, fecal calprotectin has become an integral component of modern disease monitoring strategies [5,28,31].

Despite its advantages, several challenges remain regarding the standardization and interpretation of fecal calprotectin measurements. Variability in assay methods, lack of universally accepted cut-off values, and differences in patient populations limit comparability across studies. International efforts have aimed to standardize measurement techniques and improve clinical applicability, but further research is required to fully optimize its use [5,17].

Taken together, fecal calprotectin represents a valuable, non-invasive biomarker of intestinal inflammation with well-established applications in inflammatory bowel diseases and expanding relevance in broader clinical contexts. A comprehensive understanding of its biological role, diagnostic performance, and limitations is essential for its appropriate use in clinical practice and future research.

Materials and Methods

Study design

This study was conducted as a narrative review aimed at summarizing current evidence regarding the role of fecal calprotectin as a biomarker of intestinal inflammation, with particular emphasis on its diagnostic utility, clinical applications, and emerging associations with gut microbiota and systemic inflammatory processes.

Data sources and search strategy

A comprehensive literature search was performed using the PubMed database. The search included articles published up to 2024 and was based on combinations of the following keywords: “fecal calprotectin”, “intestinal inflammation”, “inflammatory bowel disease”, “IBD”, “gut microbiota”, “intestinal permeability”, and “biomarkers”. Boolean operators (“AND”, “OR”) were used to refine the search strategy and identify relevant studies addressing both classical and emerging roles of fecal calprotectin.

Additionally, reference lists of selected articles were manually screened to identify further relevant publications. Particular attention was given to studies included in the predefined bibliography, ensuring consistency between cited evidence and the scope of this review.

Eligibility criteria

Studies were included if they met the following criteria:
(1) original research articles, systematic reviews, or meta-analyses;
(2) studies evaluating fecal calprotectin in the context of intestinal inflammation;
(3) publications addressing diagnostic accuracy, clinical utility, or pathophysiological mechanisms of calprotectin;

(4) articles available in English.

Exclusion criteria included:

(1) case reports and conference abstracts without full text availability;
(2) studies not directly related to fecal calprotectin or gastrointestinal inflammation;
(3) publications lacking sufficient methodological detail.

Study selection and data extraction

Relevant studies were selected based on title and abstract screening, followed by full-text evaluation. Data extraction focused on study characteristics, including population, study design, clinical setting, and main findings related to fecal calprotectin. Particular emphasis was placed on diagnostic performance, correlations with disease activity, and associations with microbiota and systemic inflammation.

Data synthesis

Due to heterogeneity in study design, patient populations, and measurement methods, a qualitative synthesis of the data was performed rather than a quantitative meta-analysis. The findings were organized into thematic sections, including biological function of calprotectin, diagnostic applications in inflammatory bowel diseases, differentiation between inflammatory and functional disorders, and emerging roles in intestinal barrier dysfunction and microbiota-related processes.

Ethical considerations

As this study was based solely on previously published data and did not involve direct patient participation or access to identifiable patient information, ethical approval was not required.

Limitations of methodology

The narrative nature of this review may introduce selection bias, as the inclusion of studies was not based on a fully systematic protocol. Additionally, variability in study methodologies and differences in fecal calprotectin assay techniques may affect the comparability of results across studies.

Results

Biological role of calprotectin in intestinal inflammation

Calprotectin, a heterodimer of S100A8 and S100A9 proteins, plays an active role in innate immune responses and is predominantly released by activated neutrophils during inflammatory processes [1,14]. Beyond its function as a biomarker, calprotectin has been shown to exert direct biological effects, including modulation of inflammatory signaling pathways and regulation of epithelial cell function [10,14]. Experimental studies indicate that calprotectin may influence intestinal epithelial proliferation and zinc metabolism, suggesting its involvement not only in inflammation but also in mucosal homeostasis [10]. Furthermore, neutrophil-driven mechanisms, in which calprotectin is a key component, have been increasingly recognized as

central to the pathogenesis of intestinal inflammation and its interaction with the gut microbiota [6].

Diagnostic performance in inflammatory bowel diseases

A substantial body of evidence supports the use of fecal calprotectin as a sensitive marker of intestinal inflammation in patients with inflammatory bowel diseases (IBD). Numerous studies have demonstrated a strong correlation between fecal calprotectin levels and endoscopic as well as histological disease activity [16,27]. Meta-analyses confirm its high sensitivity in detecting active inflammation, particularly in Crohn's disease and ulcerative colitis, making it a valuable non-invasive alternative to endoscopy in disease monitoring [12,29]. In addition, fecal calprotectin has been shown to be useful in predicting disease relapse, with elevated levels preceding clinical exacerbation [29]. Its role in assessing treatment response has also been highlighted, as decreasing levels are associated with mucosal healing and improved clinical outcomes [31].

Differentiation between inflammatory and functional disorders

Fecal calprotectin has proven to be an effective tool in distinguishing organic inflammatory gastrointestinal diseases from functional disorders such as irritable bowel syndrome (IBS). Studies consistently demonstrate that patients with IBS typically exhibit low or normal calprotectin levels, whereas elevated concentrations are indicative of inflammatory pathology [9,12,25]. This diagnostic utility is particularly relevant in clinical practice, where it facilitates appropriate patient triage and reduces the need for invasive procedures. Moreover, its diagnostic accuracy has been confirmed across different patient populations, including pediatric and elderly cohorts [9,12].

Clinical applications beyond classical IBD

Although fecal calprotectin is most commonly associated with IBD, elevated levels have been reported in a range of other gastrointestinal conditions. Increased concentrations have been observed in infections, colorectal cancer, and necrotizing enterocolitis, reflecting its role as a general marker of intestinal inflammation [23,35]. Additionally, studies have demonstrated its potential utility in less typical clinical settings, such as critically ill patients with diarrhea, where it may aid in identifying underlying inflammatory processes [11]. Interestingly, elevated calprotectin levels have also been reported in extraintestinal conditions, suggesting a possible link between intestinal inflammation and systemic diseases [34].

Association with gut microbiota and intestinal barrier function

Emerging evidence indicates that fecal calprotectin is closely associated with alterations in gut microbiota composition and intestinal barrier integrity. Dysbiosis has been linked to increased intestinal inflammation, with several studies demonstrating correlations between microbial imbalance and elevated calprotectin levels [19,22]. The gut microbiota influences immune activation through multiple mechanisms, including bile acid metabolism and modulation of inflammatory pathways, which may contribute to increased calprotectin release [2]. Furthermore, disruption of the intestinal barrier, often described as increased permeability,

allows for translocation of microbial products, thereby promoting low-grade inflammation reflected by elevated fecal calprotectin levels [6,20].

Methodological considerations and variability

Despite its clinical usefulness, variability in fecal calprotectin measurement remains a significant issue. Differences in sample collection methods, assay techniques, and laboratory protocols may affect the accuracy and reproducibility of results [5,11]. International consensus efforts have emphasized the need for standardization of measurement techniques and interpretation criteria to improve comparability across studies and clinical settings [5]. Additionally, the lack of universally accepted cut-off values poses challenges in defining clinically relevant thresholds, particularly in heterogeneous patient populations [17].

Limitations of fecal calprotectin as a biomarker

Although fecal calprotectin demonstrates high sensitivity for detecting intestinal inflammation, its specificity remains limited. Elevated levels may occur in a variety of conditions unrelated to IBD, including infections, malignancies, and drug-induced mucosal injury [3,35]. This lack of specificity necessitates careful interpretation of results within the broader clinical context. Furthermore, factors such as age, comorbidities, and medication use may influence calprotectin levels, potentially leading to false-positive or ambiguous findings [11].

Taken together, the available evidence supports the role of fecal calprotectin as a sensitive and clinically useful biomarker of intestinal inflammation. At the same time, its limitations and variability highlight the need for cautious interpretation and further research to optimize its application in both gastrointestinal and systemic diseases.

Results

Biological role of calprotectin in intestinal inflammation

Calprotectin, a heterodimer of S100A8 and S100A9 proteins, is a key component of the innate immune response and is predominantly released by activated neutrophils during inflammatory processes [1,14]. Its presence in the intestinal lumen reflects neutrophil migration across the mucosal barrier, which is a hallmark of active intestinal inflammation. Beyond its role as a passive biomarker, calprotectin exerts direct biological effects, including antimicrobial activity through metal ion sequestration and modulation of inflammatory signaling pathways [14].

Recent experimental studies have demonstrated that calprotectin may actively influence intestinal epithelial function. In particular, it has been shown to regulate epithelial proliferation and zinc metabolism, suggesting a role in mucosal repair and homeostasis [10]. Furthermore, neutrophil-derived calprotectin has been implicated in shaping host–microbiota interactions, potentially contributing to both protective immune responses and pathological inflammation [6]. These findings support the concept that calprotectin is not merely a marker but also a mediator of intestinal inflammation.

Diagnostic performance in inflammatory bowel diseases

Fecal calprotectin has consistently demonstrated high sensitivity for detecting intestinal inflammation in patients with inflammatory bowel diseases (IBD). Numerous studies have shown strong correlations between fecal calprotectin levels and endoscopic as well as histological disease activity, supporting its use as a surrogate marker of mucosal inflammation [16,27]. Meta-analyses have confirmed its diagnostic accuracy, particularly in identifying active disease and distinguishing between remission and relapse [12,29].

In Crohn's disease, fecal calprotectin has been shown to correlate with both colonic and small bowel inflammation, although its sensitivity may be slightly reduced in isolated small bowel involvement [15]. In ulcerative colitis, where inflammation is typically limited to the colon, fecal calprotectin demonstrates particularly strong correlation with disease extent and severity [31]. Importantly, elevated calprotectin levels have been shown to precede clinical relapse, making it a valuable predictive marker in long-term disease monitoring [29].

Additionally, fecal calprotectin has been successfully incorporated into treat-to-target strategies, where normalization of biomarker levels is used as a surrogate endpoint for mucosal healing. This approach allows for more precise disease control and may reduce the need for repeated endoscopic evaluations [5,28].

Differentiation between inflammatory and functional disorders

The ability of fecal calprotectin to distinguish between inflammatory and functional gastrointestinal disorders represents one of its most clinically relevant applications. Studies consistently demonstrate that patients with irritable bowel syndrome (IBS) exhibit low or normal fecal calprotectin levels, in contrast to patients with inflammatory bowel diseases, in whom levels are significantly elevated [9,12,25].

This distinction is particularly valuable in primary care and gastroenterology settings, where overlapping symptoms often complicate diagnosis. The use of fecal calprotectin as a screening tool enables clinicians to identify patients who require further investigation, thereby reducing unnecessary colonoscopies and improving healthcare resource utilization. Importantly, its diagnostic accuracy has been confirmed across diverse populations, including pediatric patients, in whom non-invasive diagnostic tools are especially valuable [12,24].

Clinical applications beyond classical IBD

Although fecal calprotectin is primarily used in the context of IBD, its elevation has been documented in a wide range of gastrointestinal conditions. Increased levels have been observed in infectious enterocolitis, colorectal cancer, and necrotizing enterocolitis, reflecting its role as a general marker of intestinal inflammation [23,35]. In these settings, fecal calprotectin may aid in the identification of organic pathology, although its lack of specificity limits its use as a standalone diagnostic tool.

In critically ill patients, particularly those with diarrhea, fecal calprotectin has been proposed as a marker of intestinal inflammation associated with systemic illness and gut barrier

dysfunction [11]. Furthermore, elevated levels have been reported in chronic pancreatitis, suggesting that calprotectin may reflect inflammatory processes extending beyond the intestinal mucosa [3].

Interestingly, recent studies have also identified elevated fecal calprotectin levels in extraintestinal conditions, including ophthalmological diseases such as glaucoma, supporting the hypothesis that intestinal inflammation may contribute to systemic pathophysiology [34]. These findings expand the potential clinical relevance of fecal calprotectin and highlight the need for further investigation into its role as a marker of systemic inflammation.

Association with gut microbiota and intestinal barrier function

A growing body of evidence suggests that fecal calprotectin is closely linked to alterations in gut microbiota composition and intestinal barrier integrity. Dysbiosis, characterized by reduced microbial diversity and altered composition, has been associated with increased intestinal inflammation and elevated calprotectin levels [19,22].

The gut microbiota influences immune responses through multiple mechanisms, including modulation of bile acid metabolism and production of microbial metabolites that affect epithelial function and immune activation [2]. These processes may contribute to neutrophil recruitment and increased calprotectin release. In parallel, disruption of the intestinal barrier leads to translocation of microbial products such as lipopolysaccharides, promoting chronic low-grade inflammation [6,20].

Elevated fecal calprotectin levels may therefore serve as an indirect marker of both microbiota imbalance and barrier dysfunction, linking local intestinal processes with systemic inflammatory pathways. This concept is particularly relevant in the context of metabolic diseases, where low-grade inflammation and gut-derived signals play a significant role.

Methodological considerations and variability

Despite its clinical utility, fecal calprotectin measurement is subject to methodological variability. Differences in sample collection techniques, extraction methods, and assay platforms may influence measured concentrations and affect reproducibility [5,11]. Comparative studies have demonstrated variability between different testing methods, underscoring the importance of standardized protocols [11].

International consensus statements have emphasized the need for harmonization of measurement techniques and interpretation criteria to improve comparability across studies and clinical settings [5]. In addition, the lack of universally accepted cut-off values remains a challenge, as optimal thresholds may vary depending on patient population, clinical context, and intended use of the test [17].

Limitations of fecal calprotectin as a biomarker

Although fecal calprotectin demonstrates high sensitivity for detecting intestinal inflammation, its specificity is limited. Elevated levels may occur in a variety of conditions unrelated to IBD, including infections, malignancies, and medication-induced mucosal injury [3,35]. As a result, false-positive findings may occur, particularly in patients with comorbid conditions.

Furthermore, biological variability and external factors, such as age, diet, and medication use, may influence fecal calprotectin levels, complicating interpretation [11]. These limitations highlight the importance of integrating fecal calprotectin measurements with clinical assessment and other diagnostic tools rather than relying on it as a standalone marker.

Taken together, the available evidence supports fecal calprotectin as a sensitive and clinically valuable biomarker of intestinal inflammation. At the same time, its biological complexity, methodological variability, and limited specificity underscore the need for careful interpretation and further research to optimize its clinical application.

Discussion

The present review highlights the multifaceted role of fecal calprotectin (FC) as both a biomarker and a biologically active mediator of intestinal inflammation. While its clinical utility in inflammatory bowel diseases (IBD) is well established, the growing body of evidence suggests that its relevance extends far beyond traditional gastroenterological indications. The findings synthesized in this study underscore the importance of interpreting FC not only as a diagnostic tool but also as a reflection of complex interactions between the immune system, intestinal barrier, and gut microbiota.

One of the most important observations emerging from the analyzed literature is the dual nature of calprotectin. Traditionally regarded as a passive marker of neutrophil infiltration, calprotectin is now increasingly recognized as an active participant in inflammatory processes. Studies have demonstrated that S100A8/A9 proteins are involved in the modulation of immune responses through interactions with pattern recognition receptors such as Toll-like receptor 4 (TLR4) and the receptor for advanced glycation end products (RAGE), thereby amplifying inflammatory signaling [14]. Additionally, experimental data indicate that calprotectin may influence epithelial cell proliferation and metal ion homeostasis, particularly zinc metabolism, suggesting a broader role in mucosal integrity and repair mechanisms [10]. This dual function challenges the simplistic view of FC as merely a biomarker and positions it within the pathophysiological network of intestinal inflammation.

The strong correlation between fecal calprotectin levels and endoscopic disease activity in IBD remains one of its most clinically valuable attributes. Multiple studies and meta-analyses confirm that FC reliably reflects mucosal inflammation and can serve as a surrogate marker for endoscopic findings [16,27,29]. This is particularly relevant in the context of treat-to-target strategies, where achieving mucosal healing has become a key therapeutic goal. The use of FC in this setting allows for more frequent and less invasive monitoring of disease activity, enabling earlier therapeutic adjustments and potentially improving long-term outcomes [5,28]. However, despite its high sensitivity, FC does not fully replace endoscopy, particularly in cases where precise localization or assessment of complications is required.

An important clinical strength of fecal calprotectin lies in its ability to differentiate between inflammatory and functional gastrointestinal disorders. The distinction between IBD and irritable bowel syndrome (IBS) is often challenging due to overlapping clinical presentations. In this context, FC has demonstrated high negative predictive value, making it a useful screening tool in both primary care and specialist settings [9,12,25]. Nevertheless, it should be

emphasized that borderline or moderately elevated values may still require further investigation, as they can be observed in a variety of conditions beyond IBD.

The lack of specificity represents one of the major limitations of fecal calprotectin. Elevated levels have been reported in infectious enterocolitis, colorectal cancer, necrotizing enterocolitis, and even in response to certain medications such as non-steroidal anti-inflammatory drugs [3,23,35]. This underscores the necessity of interpreting FC results within a broader clinical context. Rather than serving as a standalone diagnostic tool, FC should be integrated into a multimodal diagnostic approach that includes clinical evaluation, laboratory findings, and, when necessary, imaging or endoscopic assessment.

Beyond its established role in gastrointestinal diseases, increasing attention has been directed toward the relationship between fecal calprotectin and gut microbiota. The gut microbiome is now recognized as a critical regulator of immune homeostasis, and its dysregulation has been implicated in the pathogenesis of IBD as well as metabolic disorders [19,22]. Several studies have demonstrated associations between microbial imbalance and elevated FC levels, suggesting that calprotectin may serve as an indirect marker of microbiota-driven inflammation. Mechanistically, microbial metabolites such as bile acids can modulate immune responses and epithelial integrity, thereby influencing neutrophil recruitment and calprotectin release [2]. This highlights the interconnected nature of microbial, immune, and epithelial processes in the gut.

Another emerging concept is the role of fecal calprotectin as a marker of intestinal barrier dysfunction. Increased intestinal permeability, often referred to as “leaky gut,” has been associated with translocation of microbial products into systemic circulation, leading to chronic low-grade inflammation. In this context, FC may reflect subclinical inflammation that is not necessarily associated with overt gastrointestinal symptoms but may contribute to systemic disease processes [6,20]. This is particularly relevant in metabolic disorders such as obesity and type 2 diabetes, where low-grade inflammation plays a central role in disease pathogenesis.

The observation that fecal calprotectin levels may be elevated in extraintestinal conditions further supports the concept of the gut as a central hub in systemic inflammation. For instance, increased FC levels have been reported in patients with glaucoma, suggesting a potential link between intestinal inflammation and neurodegenerative or vascular processes [34]. While these findings remain preliminary, they open new avenues for research into the systemic implications of gut-derived inflammation and the potential role of FC as a biomarker in non-gastrointestinal diseases.

Methodological variability remains a significant challenge in the clinical application of fecal calprotectin. Differences in sample collection, storage conditions, and assay techniques may lead to variability in measured values [5,11]. Moreover, the lack of universally accepted cut-off values complicates clinical decision-making. While certain thresholds have been proposed for distinguishing between inflammatory and non-inflammatory conditions, these values may vary depending on the patient population and clinical context [17]. Standardization efforts are ongoing, but further research is needed to establish robust and universally applicable guidelines.

Another important consideration is the biological variability of fecal calprotectin. Factors such as age, diet, medication use, and comorbidities may influence FC levels, potentially leading to false-positive or ambiguous results [11]. For example, NSAID use has been associated with

increased intestinal permeability and elevated calprotectin levels, independent of underlying inflammatory disease. Similarly, transient increases in FC may occur in the context of acute infections, highlighting the importance of repeat testing in certain clinical scenarios.

From a clinical perspective, the integration of fecal calprotectin into diagnostic and monitoring algorithms represents a significant advancement in the management of gastrointestinal diseases. Its non-invasive nature, combined with high sensitivity, makes it an attractive tool for both patients and clinicians. However, its optimal use requires a nuanced understanding of its limitations and appropriate clinical context. Overreliance on FC without consideration of other factors may lead to misinterpretation and inappropriate clinical decisions.

Future research should focus on further elucidating the biological role of calprotectin in intestinal and systemic inflammation. In particular, studies exploring its interaction with the gut microbiota and its potential role in metabolic diseases are of great interest. Additionally, the development of standardized measurement techniques and the establishment of clinically relevant cut-off values will be essential for improving its utility in clinical practice.

Another promising direction is the potential use of calprotectin as a therapeutic target. Given its active role in inflammatory pathways, modulation of S100A8/A9 signaling could represent a novel approach in the treatment of inflammatory diseases. While this concept remains largely theoretical at present, it reflects the evolving understanding of calprotectin as more than just a biomarker.

In conclusion, fecal calprotectin represents a valuable and versatile tool in the assessment of intestinal inflammation. Its established role in IBD, combined with emerging evidence linking it to microbiota, barrier function, and systemic disease, underscores its importance in both clinical practice and research. However, its limitations, including lack of specificity and methodological variability, necessitate careful interpretation and highlight the need for further investigation. As our understanding of the gut–immune–microbiota axis continues to evolve, fecal calprotectin is likely to play an increasingly important role in the integrated assessment of human health and disease.

Conclusions

Fecal calprotectin is a well-established, non-invasive biomarker of intestinal inflammation with proven clinical utility in the diagnosis and monitoring of inflammatory bowel diseases. Its strong correlation with mucosal inflammation and its ability to differentiate between inflammatory and functional gastrointestinal disorders make it an important tool in contemporary clinical practice.

At the same time, fecal calprotectin is not a disease-specific marker, and its levels may be influenced by a variety of conditions, including infections, malignancies, and medication use. Therefore, its interpretation requires careful consideration of the clinical context and should be integrated with other diagnostic modalities.

Emerging evidence suggests that fecal calprotectin reflects broader aspects of intestinal homeostasis, including interactions with gut microbiota and intestinal barrier function. This

expands its potential role beyond classical gastrointestinal diseases and highlights its relevance in systemic inflammatory and metabolic conditions.

Despite its advantages, limitations such as methodological variability and lack of standardized cut-off values remain significant challenges. Further research is needed to optimize its clinical application, improve standardization, and explore its potential role as both a biomarker and a therapeutic target.

Overall, fecal calprotectin represents a valuable component of modern diagnostic strategies, with growing importance in the integrated assessment of intestinal and systemic inflammation.

Disclosure

Supplementary Materials

There are no supplementary data connected with this article.

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The authors declare no conflicts of interest.

Declaration of the Use of Generative AI and AI-Assisted Technologies in the Writing Process

During the preparation of this work, the authors used Grammarly for the purpose of improving language and readability. After using this tool, the authors reviewed and edited the content as needed and took full responsibility for the substantive content of the publication

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