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Multi-Matrix 5-Aminosalicylic Acid Efficacy in Induction of Remission in Mild-to-Moderate Ulcerative Colitis: A Systematic Review

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Abstract

Background and Aim: The development of new technologies for ulcerative colitis such as the matrix form of 5-aminosalicylic acid or mesalazine has already shown efficacy over placebo, but not over coated tablet form, which is usually used in clinical protocols for this disease management. Thus, this trial aimed at carrying out a systematic review to gather evidence that can reveal pre-eminence or equivalence in efficacy and safety of these two pharmaceutical forms in induction of remission in mild to moderate ulcerative colitis. **Methods:** Two independent researchers using Pubmed, Embase, Web of Science, Clinical Trials, Scopus and Science Direct databases and manual search selected eligible randomized clinical trials according to some pre-established inclusion criteria. This research was carried out from July 2016 to April 2019 without limitation of time interval or language, using clinical and endoscopic remission rates as primary endpoints of analysis. **Results:** Three studies met inclusion criteria and results have demonstrated that similar levels of endoscopic remission were achieved in both forms of the drug. However, clinical remission rates have suggested better results when mesalazine matrix was used. On the other hand, adverse effects were similar in both formulations, with headache and gastrointestinal disorders as the most representative ones. **Conclusion:** It was concluded that there are insufficient clinical studies to demonstrate the superiority of 5-ASA multi-matrix when compared with coated tablet during ulcerative colitis treatment. Consequently, it requires further clinical studies to add a deeper discussion on choosing a better therapy that can handle with this kind of disease.

Keywords: Mesalazine, Multi-Matrix System, MMX 5-Asa, Systematic review, inflammatory bowel diseases.

1. Introduction

Ulcerative colitis (UC) is an inflammatory bowel disease, whose symptoms are associated to episodes of bloody diarrhea and intense abdominal pain[1]. Its epidemiology incidence has been under development, especially in developing countries in Latin America and Asia[2] due to several factors that may influence in its spreading out such as economic growth, changes in diet, exposure to drugs and substances and changes in stress levels[3].

The treatment of UC patients is based on a diet that aims at constipating the gastrointestinal tract in order to reduce evacuation frequency[4], as well as the use of drugs that may induce the disease remission and control symptoms[5]. Among drugs, 5-aminosalicylic acid (5-ASA) or mesalazine has been extensively taken since there is a better safety profile when compared with corticosteroids or immunosuppressants[6]. Action mechanism of mesalazine has not been established yet, but it is known that, besides inhibiting cyclooxygenase type 2, mesalazine can inhibit leukocyte's mobility[6]. It has antioxidant properties[7]; it is able to prevent mitochondrial damage[8] and it inhibits some transcription factors of pro-inflammatory substances such as NF-Kb[9].

The dose and pharmaceutical form have the main role on aminosalicylates efficacy, especially 5-ASA. Among the available ones, coated tablet is the most widely taken during UC-patients' treatment. However, innovative formulations such as Multi-Matrix System® (MMX®) have already proved their efficacy against placebos[10-12] with the maintenance of beneficial effects up to 12 months[13].

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Multi-matrix mesalazine has some advantages regarding adherence to treatment due to the lower frequency of daily administrations[14]. In addition, MMX® system reaches further parts of the intestinal tract due to hydrophilic and lipophilic constitution in a single tablet, which allows a slow and gradual release of the active principle, consequently extending its therapeutic effect[15]. Since adherence is one of the determining factors for the success of this therapy[16], and considering that the addition of this kind of drug improves individuals' lives who suffer with UC, it can be extremely worthy and important. However, there are no studies yet to gather evidence concerning the superiority or efficacy of multi-matrix technology over conventional treatment that has been currently applied.

2. Methods

A systematic review was carried out by two independent researchers from July 2016 to April 2019, following the criteria recommended by the updated version of the Cochrane Handbook for Systematic Reviews of Interventions and using the checklist proposed by PRISMA methodology (Main Items for Reporting Systematic Reviews and Meta-analyses). The accessed databases were: Pubmed, Embase, Web of Science, Scopus and Science Direct. The selected keywords were: MMX mesalazine, MMX mesalamine, MMX 5-ASA, MMX aminosalicylic acid and mesalazine multi-matrix, ulcerative colitis, UC, colitis, ulcerative, efficacy and randomized controlled trial, so that they were combined with the Boolean operators "And" and "Or". The clinical trials registered in the Clinical Trials database were also researched in order to find out unpublished studies. Also, an additional research in "The Cochrane IBD / FBD Group Specializes Trials Register" was carried out to ensure the originality and exclusivity of this research. In addition, a manual search of relevant references has also been done to fulfill any doubts.

All prospective, randomized, double-blind, exclusively human studies were included, with no age or gender limit. They associated mesalazine use in matrix system (MMX®) from 1.6 to 4.8g dose to be compared with a 5-ASA tablet (Asacol® Procter & Gamble, Cincinnati, OH), whose dose ranged from 0.4 to 0.8 g. Studies with no defined outcome did not take part of this research, neither the ones from symposiums or congress nor those ones that did not comply with the inclusion criteria mentioned above. The following outcomes were considered as positive conclusions: a) Clinical remission (analyzed during a medical evaluation and/or a subjective evaluation by the patient/studied participant); b) Endoscopic remission and maintenance of endoscopic remission (improvement of mucosal appearance in imaging tests – sigmoidoscopy/colonoscopy/ endoscopy - according to the medical examiner criteria).

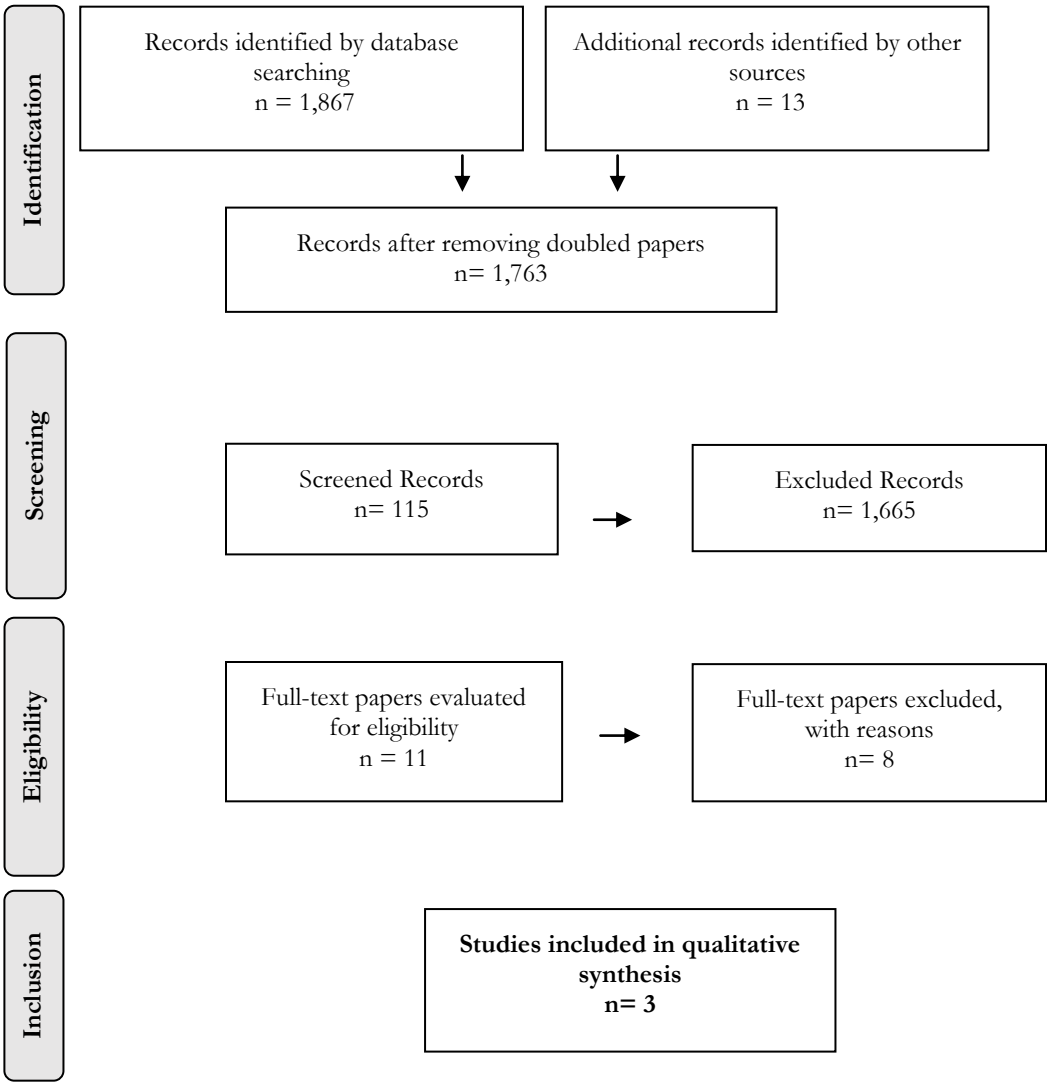
Secondly, the time of relapse was also analyzed (interval between the day of randomization until the occurrence of some serious symptom that leads to the withdrawal of some participants of any group from the experiment due to the efficacy lack) as well as tolerability and safety, including observed adverse effects and their frequencies, drug-related adverse events, and occurrence of severe adverse events and side effects.

The quality of selected papers was analyzed based on the method proposed by Jadad et al.[17], which mainly qualifies methods such as randomization, blinding and description of exclusions and losses. In addition, their quality was also analyzed by the items included in Cochrane Collaboration tool at Review Manager version 5.3 (random sequence generation, allocation concealment, participants' and personnel's blinding, outcome assessors' blinding, incomplete outcome data, selective reporting and other sources of bias). The results were analyzed based on the construction of tables that related the year of each study, authors, kinds of intervention, number of participants, kind of analysis for outcome and result concerning the use of multi-matrix system as the main stream of oral 5-ASA agent for UC treatment.

3. Results

The information flow of this research is shown in Figure 1. A total of 1,880 papers were registered, including those from databases and manual research, and after excluding doubled papers, there were 1,763 studies to be analyzed. Finally, 115 reports were screened during the selection phase, consequently, eleven documents were entirely read and reviewed.

Figure 1: Systematic Review's flow diagram



Finally, eight papers were excluded based on the inclusion criteria: two of them did not publish the results; two were abstracts in scientific congresses, one of them was a clinical trial without comparative factor, two of them were compared with placebos and one was a systematic review whose theme did not meet with this research. And, three studies were included in this review, according to pre-defined inclusion rules[15,18,19].

Regarding the methodological quality of the studies, the three selected studies showed low risk of bias in general. However, one of the papers[19] did not reveal how it avoided the trend of results and outcomes. Besides, according to the Review Manager tool, in "Other sources of bias" item - in which conflicts of interest and financing fit - only one study[15] did not provide essential information to be considered as low risk of bias. However, these data do not deny the use of included studies. And, according to Jadad and collaborators[17] evaluation scale, all the papers reached maximum score by the proposed evaluation methodology.

3.1 Patient demographics and Interventions

During this research, 1,108 individuals were analyzed in three eligible studies, which were separated into "MMX Group", for participants who used the matrix tablet during the experiment, "Asacol Group" (0.4 g or 0.8 g coated tablet of 5-ASA) and placebo group, and this last one was present in a study[15]. According to Kamm and collaborators[15], there is also the designation of MMX1 and MMX2 since there are two groups of patients using multi-matrix form, at 2.4 g and 4.8 g dose, respectively.

Regarding the selected medical centers, all the studies were multi-centric, and one of the studies[18] recorded centers in Italy, Ukraine and Poland. Another study[15] also took part in Germany, Spain, France, Poland, Hungary, Russia, Israel, Latvia and Lithuania; and the third one included[19] a trial with one hundred and thirteen centers, distributed in twenty-seven countries in the American, Asian, European, African and also in Oceania continents.

Two studies[15,19], related to the obtained results, analyzed only the outcomes based on the researchers' perspective. Analyses such as sigmoidoscopies, laboratory tests, vital signs evaluation and symptoms for D'Haens and collaborators[18] occurred in the first, second, fourth and eighth weeks of the experiment. While Kamm et al.[15] analyzed the same parameters in the first, third and sixth month of the clinical study.

Prantera et al.[18] presented the outcomes based on two perspectives: the first one was entirely based on the investigators' analyses, which happened every three, six, nine and twelve months after randomization, through interview and sigmoidoscopy exams; while the second one was based on subjective analysis of the participants. They had a notebook where they reported their observations (such as side effects, worsening of symptoms and increase of evacuation frequency) during all the days of the experiment. This was a strategy to record the changes that were not identified when they went to the physician appointment again. Table 1 lists the reports, number of each participant, kinds of intervention and design of included studies.

Table 1: Systematic review's included studies.

Author, year	Duration	Participants	Intervention	Method
Kamm et al., 2007	2 months	212	MMX 1 Group: 2 tablets of MMX® 5-ASA† 1.2 g once a day. MMX 2: 4 tablets of MMX® 5-ASA 1.2 g once a day Asacol Group: 2 coated tablets of 5-ASA 0.4 g (Asacol®) three times a day Placebo Group‡	Multicentric, Randomized, Double-blind
Prantera et al., 2009	12 months	217	MMX Group: 2 tablets of MMX® 5-ASA 1.2 g in the morning + 1 tablet of placebo at night. Asacol Group: 2 coated tablets of Asacol® 0.8 g in the morning + 1 coated tablet of 5-ASA 0.8 g at night.	Multicentric, Randomized, Double-blind
D´Haens et al., 2012	6 months	679	MMX Group: 1 tablet of MMX® 5-ASA 1.2 g + 1 tablet of placebo in the morning and at night Asacol Group: 2 coated tablets of 5-ASA 0.4 g + 2 tablets of placebo in the morning and at night. Placebo Group‡	Multicentric, Randomized, Double-blind

† 5-Aminosalicylic acid
‡Not described in the study the form of placebo administration.

The patients' distribution with divergence of sex, age, lifestyle (people who smoke and exercise) or anatomical localization of inflammation was homogeneous in all studies. There was a single study[19] that stratified the obtained results by describing the difference between primary and secondary outcomes in relation to sex, ethnicity, life history (smoking history or not) and anatomical localization of UC, whereas two other studies[15,18] only described that the outcomes showed no discrepancy between the analyzed groups.

3.2 Endoscopic remission

Endoscopic remission was considered when, according to the diagnostic imaging parameters, there was some improvement in mucosal appearance or intestinal scarring when compared with an initial evaluation at randomization (day 1 of drug administration). The results are shown in Table 2.

Table 2: Included studies and their respective endoscopic remission rates.

Author, year	Endoscopy/ Sigmoidoscopy	EndoscopicRemission(%)			Conclusion
		MMX		Asacol	
Kamm et al., 2007§	First, second, fourth and eighth weeks of the experiment	69%†	77.6%‡	61.6%	MMX Group = Asacol Group*
D'Haens et al.,2012¶	First, third and sixth months of experiment	83.7%		81.5%	MMX Group = AsacolGroup**

ConfidenceInterval (CI)= 95%
†Administration of 2.4 g/day of multi-matrix 5-ASA
‡Administration of 4.8 g/day of multi-matrix 5-ASA
§Endoscopic remission defined as at least a 1-point reduction from baseline in sigmoidoscopy score (1= erythema, decrease vascular pattern, minimal granularity; 2= marked erythema, friability, granularity, absent vascular pattern, bleeding minimal trauma, no ulcerations; 3= ulcerations, spontaneous bleeding)
¶Endoscopic remission defined as a modified UC-DAI endoscopy sub-score ≤ 1 point based on a score of mucosal appearance (0= normal; 1= erythema, decreased vascular pattern, and minimal granularity; 2= marked erythema, friability, granularity, absent vascular pattern, bleeding with minimal trauma, and no ulcerations; 3= ulceration and spontaneous bleeding)
*$p \leq 0.05$
**p value not described.

Only two reports, Kamm et al.[15] and D'Haens et al.[19], used this parameter of analysis. Both studies reported that endoscopic remission rates for both multi-matrix and coated tablets reached similar endoscopic remission rates, so that more than half of the population in each group achieved an improvement in intestinal mucosa aspect and, consequently, was closer to some symptom relief, extension and severity of UC.

D'Haens et al.[19] also evaluated endoscopic remission in stratified groups. Each patient had an individual endoscopic examination on the first day of randomization, which allowed researchers to score them according to the mucosa aspect. Among these scores, some individuals scored 1 for endoscopy, which meant a mucosa with erythema and slight granularity. But, the others in which the score was 0, it corresponds to normal appearance.

This second group, therefore, took part of individuals with better intestinal conditions since the beginning of the experiment. According to the answers from "MMX group", researchers registered better remission rates in participants with score 0, when they were compared with those ones with mild mucosal changes (86.3% vs. 84.3%, CI=95%). This showed that multi-matrix tablet may possibly be more effective in that kind of patient.

The same study also analyzed if there were influences of characteristics such as sex, ethnicity, smoking habit and anatomic area of the disease and it was observed that, in individuals who were Caucasian, there were better indices when doses of coated tablets of mesalazine were administered, as in those individuals with a history of smoking and specific anatomical area (distal ulcerative colitis). Regarding participants with no history of smoking, but with a diagnosis of disease in other anatomical areas, better results were obtained during the administration of multi-matrix tablets.

3.3 Clinical remission

Regarding clinical remission, the authors used different parameters to access it. According to Kamm et al.[15], it was defined as a modified UC-DAI score of ≤1, with zero score for rectal bleeding and stool frequency and at least 1-point reduction from baseline in sigmoidoscopy score. But, based on this study results[15], better rates are achieved when matrix technology was used at, for example, 2.4-g daily (41.7%) and 4.8-g daily (41.2%) concentrations when compared with Asacol® (33.7%). According to Prantera et al.[18], clinical remission was defined as a combined score of ≤ 1 on UC-DAI scale, whose combined score was the total of investigator's assessment based on patient's condition, stool frequency and rectal bleeding, and only one of these three components could have one as value. In this study, there was no statistic significant difference on investigator's unique analysis (68% vs. 65.9%, $p = 0.69$) regarding clinical remission index between "MMX group" and "Asacol group".

However, when this evaluation is combined with the participants' notebooks information, there is an important difference (p = 0.05), since 62.2% of participants who used the matrix technology achieved clinical remission, while in "Asacol group", 51.5% of individuals achieved remission. D'Haens et al.[19] did not use clinical remission as a parameter of analysis. However, they presented important data on the analyzed factors at UC-DAI scale during six months of this study, when compared to the participants' score between randomization and the sixth month of the clinical trial. According to the results, the number of participants who scored zero (0) was lower after the sixth month of study in both matrix tablet group and mesalazine-coated tablet one (Table 3).

In addition, no participant showed scores higher than two (>2) and lower than three (<3) during the randomization day, but at the end of the six months of treatment, both groups registered participants with such score (Table 3). There was an increase of patients with worse clinical status related to the drop-outs throughout the study, which were not related to drug administration.

Table 3: UC-DAI participants' scores between randomization and the sixth month of study.

UC-DAI score†	Randomization		Sixthmonth	
	MMX Group‡ (n; %)	AsacolGroup§ (n; %)	MMX Group (n; %)	AsacolGroup (n; %)
0	286 (83.4)	268 (72.6)	249 (72.6)	240 (71.2)
2 to<3	0	0	3 (0.9)	2 (0.6)

ConfidenceInterval (CI)= 95%
† UC-DAI= Ulcerative Colitis Disease Activity Index
‡Administration of multi-matrix 5-ASA (2.4 g)
§ Administration of 5-ASA coated tablet (1.6 g)

There was some relevant information obtained from a certain study[18] with different participants' ratio regarding clinical remission achievement, according to the centers from which they took part. The remission index was higher in areas such as Poland and Ukraine, when compared to the individuals who were studied in group from Italy. This, according to the authors, reflects the divergent health service practices among these countries, so that in Italy there were more individuals undergoing appropriate treatment, while in Poland and Ukraine, the analyzed patients did not receive an effective therapy for UC treatment.

3.4 Combined clinic and endoscopic remission

There was a combination between UC-DAI scale analysis and the result of sigmoidoscopy carried out in the last month of the study in a research during the first decade of 2000[15,18]. The analysis aimed at correlating endoscopic and clinical remission rates in order to verify whether they increase or decrease proportionally.

According to Kamm et al.[15], the use of MMX®mesalazineat 2.4 g achieved a greater remission rate when compared with placebo (40.5 vs 22.1%, p = 0.010), as well as at 4.8-g dose (41.2 vs 22.1%, p = 0.007). While individuals that took the coated tablet did not achieve this statistically significant parameter when compared with placebo (32.6 vs 22.1%, p = 0.124). Yet, the researchers compared indices between matrix technology and the directly coated tablet, and there was a considerable difference between the obtained remissions. Thus, this answer showed that better results were recorded when MMX®mesalazine tablet was administered.

According to Prantera et al.[18], 60.9% of participants from "MMX group" were in clinical and endoscopic remission, while in "Asacol group", 61.7% of them were in the same situation, although there was no significant difference (p = 0.89). When the participants' notes were considered, the achieved remission rates were lower and again without statistically significant difference (55.8 vs. 48.5%, p = 0.19).

3.5 Relapse Time

According to D'Haens et al.[19] study, disease relapse was related to dropouts during the experiment. The authors also found out that there was no statistical difference on relapse rates due to disease relapses between "MMX group" and "Asacol group" (12.8 vs. 14.6%, p= 0.516). For Prantera et al.[18], the evaluation of relapse time between both groups was not significant when the analysis was exclusive to the researcher (p= 0.48), but there was a significant difference when the participants' private analysis was included (p = 0.031).

3.6 Safety

Kamm et al.[15] reported 115 adverse effects (AEs) in 72 participants. They occurred homogeneously among the studied treatments, with no difference between the occurrences in "MMX group" and "Asacol group". Prantera et al.[18] identified 191 AEs in the total (56.8% in "MMX group" and 58.6% in "Asacol group"). And according to D'Haens et al.[19] study, there was also a statistical similarity of occurrence in both groups, so that 37.1% of individuals in "MMX group" and 36.0% in "Asacol group" underwent these events.

In the three included studies, bowel problems (with UC relapse as the main representative) and central nervous system disorders (the main manifestation was headache) were the most common AEs, and as the authors explained, none of them was dose-dependent. Severe adverse effects (SAEs) (any medical event that results in hospitalization, persistent disability or that causes any congenital problem) have also been investigated in the included studies and are described in Table 4.

Table 4: Severe adverse effects identified in the included studies.

Author, year	**"MMX Group" SAEs† (n)**	**"Asacol Group" SAEs (n)**	**SAEsrelatedtotreatment**
Kamm et al., 2007	1‡	2	Notrelated
Pantera et al., 2009	6	5	MMX group: melena Asacol group: epistaxis and increase of pancreatic enzymes
D'Haens et al., 2012	6	3	Notrelated

†Severe adverse effects
‡Administration of multi matrix 5-ASA 2.4 g/day

Among the identified SAEs, gastrointestinal events were predominant, although UC was the most common one. According to Kamm et al.[15] and D'Haens et al.[19], no SAE is related to the dose forms of mesalazine, whereas for Prantera et al.[18], melena occurrence is related to 5-ASA multi-matrix use and the use of coated tablet is associated to epistaxis occurrence and increase of pancreatic enzymes. The number of dropouts was also analyzed due to the treatment, so D'Haens et al.[19] study, showed a greater number of dropouts from the experiment in "MMX group" in relation to "Asacol group", but none of them was related to the use of the proposed treatments.

4. Discussion

Regarding therapeutic efficacy, endoscopic evaluation reveals that both matrix form and 5-ASA modified release coated tablets are able to achieve remission at important levels, whose efficacy rates were statistically similar. Interchangeable data have been reported in a meta-analysis in 2016[20]; however, even with a result that is not considered representative for a big population, a single study included in this systematic review[18] has demonstrated that when the patient's perspective is considered, the results can provide value data regarding life quality, as clinical remission is as important as the endoscopic one.

Janke et al.[21] found out that decrease on symptoms severity of inflammatory bowel diseases is a crucial pre-existing factor that may predict an increase in patients' quality of life, which was later analyzed and attested by Solomon et al.[22] as well as by Hodgkins et al.[23]. Besides, the relevance of a clinical remission analysis ensures that evolution in remission of a disease is indeed positive, since the readings of endoscopies, sigmoidoscopies and imaging tests in general may suffer discrepancies between one analyzer and another due to subjectivity of analysis, as reported by D'Haens et al.[19]

The analysis of symptoms may also be important to anticipate the anatomical area in which lesions can be observed, as it is shown by Osada et al.[24] in their study. The authors recorded that intensification of clinical UCmanifestations mainly reflect the severity of distal lesions. Since multi-matrix technology is able to reach more distant areas due to its release form, it is suggested that the choice of this technology would achieve better results.

Adherence to this kind of treatment is also an important factor of analysis that, even though it is not treated in clinical studies, it can be suggested based on other literatures. As previously reported in a systematic review[25], there is a large disparity between adherence analyzed in randomized clinical trials and actual occurrence during outpatient therapy established for patients to treat UC, so that the requirement of clinical evaluation and endoscopy in short periods of time influence greater use and correct administration of drugs, which does not necessarily reflect in the actual habit of drug consumption after an established therapy.

For this reason, the multi-matrix form has a slight advantage over the coated tablet since, once the single daily administration of any drug is enough to get satisfactory results, adherence to the treatment of this kind of therapy is greater, as already reported by Lichtenstein[26]. Adherence has also influenced the chronic way of this disease, since anyone who remains in continuous and correct use of mesalazine to treatUC has lower chance of developing colorectal cancer[27]. Besides, adherence may also influence some outlay on therapy, as observed by Kane et al.[28] in their experiment, which demonstrates that adherence to therapy may decrease recurrence rates, and, thus, reduce hospitalization and acquisition processes of other drugs to control the disease, so, consequently there is a reduction on expenses.

In addition, the American Gastroenterological Association has published a new Clinical Practice Guidelines on the Management of Mild-to-Moderate Ulcerative Colitis[29], which has suggests that, in patients with mild-moderate UC treated with oral forms of 5-ASA, it is better to give a daily dose than multiple ones a day. It is important to highlight that both profile and design of the included studies have revealed some similarities, mainly on how a patient is selected (all studies were multi-centric and with homogeneous demographic profile). The demonstration of results using UC-DAI scale as the main form to evaluate patients' symptoms in clinical remission and sigmoidoscopy is the most representative imaging test on endoscopic remission evaluation. Also, according to the included experiments, there is no difference in mesalazine action in its multi-matrix form with different populations, regardless of age or sex. These results are consistent with those ones that were found out by Lichtenstein et al.[12], who verified that sex, extent or different levels of this disease do not influence the percentage of endoscopic or clinical remission.

However, doses used between one study and the other were in fact divergent due to some clinical treatment protocols at each area or due to regulatory requirements. This happened in D'Haens et al. study[19], in which the maximum dose of Asacol® was 1.6 g/day/requirement according to the Food and Drug Administration (FDA). So, it was impossible to match doses between matrix-based and conventional tablets.

The adverse effects were also very similar between both pharmaceutical forms, and they also showed UC relapse and headache as main representatives, consequently, safety and tolerability profiles are equivalent. There was quality on the studies, since, when both parameters of evaluation concerning methodological quality are combined to be used in this review, it can be inferred that the three studies have little bias chance in relation to patients' allocation, results and participants' blinding. However, even with good results of efficacy, induction and maintenance of remission in UC[30], few studies have already evaluated 5-ASA matrix in comparison with conventional treatments, which contributes to the reluctance on using this pharmaceutical form. The lack of clinical studies reflects not only efficacy doubts, but also some restriction on suggesting some drug mainly to patients whose financial conditions are less available concerning the high cost of matrix technology.

Brereton et al.[31] and Yen et al.[32] carried out drug-economic studies that described advantages on using multi-matrix tablets in relation to conventional technology. This evidences that even with extra pharmaceutical costs, the benefits related to drug adherence led to a reduction in hospitalization expenses, which also increases the chances of a better cost-effectiveness relation. However, matrix technology still has limited application mainly because of its cost, since it is mostly used by patients with higher purchasing acquisition[32]. Even though therapeutic decision making has been suggested by official protocols in UC patients' management, it can be favored due to the different forms of mesalazine presentation. It should be highlighted that factors such as purchasing acquisition, treatment accessibility and adherence to this therapy must be considered.

5. Conclusion

During this study, it could be observed that multi-matrix technology was well supported, since the efficacy on 5-ASA MMX® tablets is very similar to the one on the conventional coated tablet, but the matrix technology points out better results in the remission parameters clinic. In addition, safety profile of both dose forms was also equivalent. However, choosing matrix technology as the main way to combat UC is still controversial due to the high cost of this pharmaceutical form.

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Conflict of interests

The authors declare that have no industrial links or affiliations and there's no conflict of interest for the publication of this article.

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