Maggot Therapy for Removal of Non-healing Wounds

Lisa Bekins
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Maggot Therapy for Removal of Non-healing Wounds

Abstract
Background: Maggot therapy has been used for centuries for treatment of non-healing soft tissue wounds. Maggot therapy disappeared for a while due to newly available antibiotics and improved surgical techniques. Recently it has made a comeback and is now considered medicinal maggots. The clinical question of whether to use maggot therapy for the treatment of non-healing wounds in comparison to more standardized therapy is resurfacing among clinicians and patients.

Methods: A systematic review of current literature over the last 10 years on the efficacy of maggot debridement therapy was conducted through an extensive online article search using MEDLINE, CINAHL, and EBM reviews.

Results: Of the five studies that were evaluated in this review, all showed that maggot debridement therapy was effective in debriding wounds more quickly than conventional treatment. Healing time was either equal to or shorter than standardized methods. There were quite a few limitations such as the inability to carry out randomized controlled trials, inadequate number of articles found and a small number of subjects integrated in each study.

Conclusion: Studies in the past prove that maggot therapy is effective in debridement of non-healing chronic wounds. This leads to enhancement of healing time and suggests that this technique is an effective and safe method of debridement for patients that are appropriate for this treatment.

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Maggot Therapy for Removal of Non-healing Wounds

Lisa Bekins

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Clinical Graduate Project Coordinators: Annjanette Sommers MS, PAC & Rob Rosenow PharmD, OD
Biography

[Redacted for privacy]
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To my parents: Thank you for your constant support and understanding. Dad, thank you for pushing me to be the best person that I can be. Mom thank you for showing me what real strength is, your battle to overcome breast cancer drove me into medicine.

To my brother: Thank you for always being there to support me.

To my grandparents: Thank you for helping me through P.A. school. Grandma, thank you for reminding me how important this is to me- I miss you.

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Table 1: Summary of Clinical Trials Reviewed

List of Abbreviations

MDT…………………………………………………………Maggot debridement therapy
CI.............................................................................................Confidence Interval
PVD…………………………………………………………Peripheral Vascular Disease
MRSA………………………………………………………Methicillin-resistant Staphylococcus aureus
Maggot Therapy for Removal of Non-healing Wounds

BACKGROUND

Maggot therapy has been used for centuries. It was first acknowledged by military surgeons who noted faster healing of wounds with maggots.1 Baer was the first to promote and document the use of maggots for treatment of wounds in the US during the 1920s and 1930s.1-2 Starting in the 1940s there was a decrease in the usage of maggot therapy due to the availability of antibiotics and more efficient surgical techniques.2-3 Maggot therapy became more popular in the 1980s and 1990s, when various wound treatments led to the need for more research in the area.3 Recently an increase in antibiotic resistant strains of bacteria and in diabetic foot and pressure ulcers2-3 led to the FDA, in 2004, granting permission to produce and market maggots for prescription use. This treatment is recommended for “non-healing necrotic skin and soft tissue wounds such as venous stasis ulcers, diabetic foot ulcers, pressure ulcers and non-healing traumatic or post surgical wounds.”4-5

Debridement is defined as the removal of dead or necrotic tissue to prevent infection and to improve healing, to avoid wound delay which would provide a breeding ground for bacteria leading to gangrene, probable amputation and possible septicemia.6 There are different types of debridement such as surgical (sharp), mechanical, autolytic and biological. Biological is the usage of sterile maggots for debridement.7 The maggots that are typically used are the larvae of Lucilia sericata that come from the greenbottle fly.2 They usually travel in masses that secrete digestive enzymes and spread putrefying bacteria.8 Maggots perform three mechanisms of action: they clean wounds by dissolving dead and infected tissue, they disinfect the wound, by killing the bacteria and they stimulate wound healing.9 Larvae clean the wound both by mechanically scraping the wound and by secreting digestive enzymes that liquefy and dissolve the dead tissue. Once identified by the maggots the dead tissue is drained from the wound. In terms of disinfection, the maggots eradicate the bacteria through ingestion, degradation and by secreting potent antimicrobial material.10 The wound healing aspect of the process
is still not completely understood although many studies have potentially attributed this to secretions that stimulate growth of granulation tissue such as allantoin.\textsuperscript{11}

Maggots are applied to the wound directly usually in groups of 5-10 larvae/cm\textsuperscript{2}. They are held in place for two to three days until the debridement is completed and the maggot is satiated. Care is taken not to allow the maggots to remain in place long enough to cause pain to the patient.\textsuperscript{6} This process can be repeated multiple times with a new group of maggots until the necrotic tissue is cleared away, the bacteria is gone and healthy granulation tissue starts to grow.\textsuperscript{12} Maggots are usually contained in the wound by a cage-like dressing, which is typically a porous, mesh covering to allow air and drainage of liquefied necrotic tissue.\textsuperscript{2}

Maggot therapy is currently considered the last resort for treatment of wounds. It is used when other treatments have failed, when surgery is not an option, or when cost is an issue.\textsuperscript{9} Larvae usually cost $80- $110 per vial making it a very cost effective treatment.\textsuperscript{13} One obstacle is overcoming the fear of maggots. Interestingly, it is the providers rather than the patient that seem to have the greatest anxiety about the treatment. Patients come to accept the idea quite easily because of the invasive nature of the alternatives but they still suffer from a common misconception that the larvae will turn into a fly during the treatment.\textsuperscript{12-13}

Most of the research either focuses on specific types of wounds that are treated by both maggot therapy and conventional treatments, or multiple wound types grouped together. The purpose of this systematic review is to determine the efficacy of maggot debridement therapy compared to other treatments and to assess whether it could be used as a first line therapy for treatment of non-healing wounds.
METHODS

A comprehensive literature search was compiled using the keywords: larva, maggot therapy, debridement, and wound healing. These terms were searched separately as keywords, then combined to form a single search using the “and” command. Bibliographic databases used were Ovid-Medline, CINAHL, Evidence-Based Resources, and Google scholar. Literature was reviewed by title and abstract, and then weighted towards importance at answering the clinical question. Relevant articles were then compiled and analyzed. Data was limited to the last two decades, using only human subjects with an additional search filter for randomized control trials.

The inclusion criteria were published randomized controlled trials and prospective and retrospective studies comparing the effectiveness of maggot therapy debridement in comparison to standardized treatments. Studies were published in English. The studies involved only the Lucilia sericata larvae.

Individual case studies, multiple case series and systematic reviews were excluded as were studies examining people with allergies to hydrogel or other treatments. Wounds likely to communicate with a large blood vessel, body cavities or vital organs were excluded. Wounds that were life or limb threatening were also excluded.

RESULTS

A total of five published articles addressed the issue of whether maggot debridement therapy was effective and met the inclusion and exclusion criteria for the systematic review (Table 1). There is one randomized controlled trial, a cohort study, a multivariate analysis, a case control study and a chart review.14-18

In 2002, Sherman14 performed a cohort study of maggot therapy for the treatment of pressure ulcers. This was compared to conventional therapy in 103 patients with 145 pressure ulcers from 1990 to 1995. Maggot therapy was applied to the ulcer using 5-8 larvae/cm². A cage like dressing was
created with a hydrocolloid ring and porous Dacron sheet or nylon stocking. Next a gauze pad was placed on top, which was replaced frequently due to profuse amounts of drainage. Cycles were 48 hours long and it was typical to apply two cycles per week with a saline – or 0.125% sodium hypochlorite moistened gauze dressing used in the time between the cycles. Conventional therapy consisted of topical antimicrobial therapy, multiple combinations of nonsurgical treatments, acemannan and hydrogels, saline-moistened or wet to dry dressings, chemical debriding agents, hydrocolloids and calcium alginates and growth factors.14

Digital photographs were taken to measure ulcer length, width, surface area and circumference. The main conclusions were quantification of debridement and wound healing and wound size. Sixty-seven patients with 92 wounds met all of the inclusion and exclusion criteria and most were diabetics or had spinal cord injuries. A total of 43 wounds were treated with MDT and 49 wounds received conventional therapy. Maggot debridement therapy worked on larger wounds and debrided the wounds quickly and more completely than the standardized therapy. In less than five weeks, the ulcers treated by maggot therapy were 80% debrided and 52% of conventionally treated wounds were not completely debrided in a 5.5 week period (P=0.021). When looking at necrotic tissue, repeated measures analysis of variance was used that showed maggot therapy decreased necrotic tissue significantly with a decrease of 3.7cm² within the first two weeks. There was no significant change in necrotic tissue of the wounds treated by conventional therapy within that time period. Healthy granulation tissue grew more rapidly in wounds treated by maggot debridement therapy then by conventional therapy (49% vs. 18%, P=0.002).14

In 2003, Sherman15 performed another study looking at the effectiveness of treating diabetic foot and leg ulcers with maggot therapy. It compared this treatment to conventional therapy in 18 diabetic patients with non-healing wounds. These patients were selected from 143 maggot therapy applicants between 1990 and 1995. Within the first two weeks, if the wounds had not healed and could be measured by planimetry then they were included in the study. Six wounds were treated with
maggot therapy, six others were treated with conventional therapy and eight wounds were treated with conventional therapy first and then maggot therapy. Maggot therapy consisted of sterile Lucilia sericata larvae, 5-8 larvae/cm² placed directly into the wound by loose sterile gauze. A hydrocolloid pad was placed around the wound margins with a central hole cut to protect the surrounding skin. Then a porous Dacron chiffon or nylon stocking was taped or glued to the hydrocolloid ring to create a cage for the maggots. An absorbent gauze pad was placed on the top to soak up the drainage from the necrotic tissue. The maggots were replaced in cycles of 48 hours but the top layer was removed every 4-6 hours when soiled. Each week, one to two cycles of maggot therapy was applied and saline- or sodium hypochlorite- drenched gauze was placed on the wound between these cycles and after the treatment was accomplished. The patients receiving conventional therapy had a regimen chosen by their primary care or wound care providers. The types of conventional therapy chosen were non-medicated dry dressings or saline-moistened wet-to-dry dressings changed every 8 hours, topical antimicrobials, hydrogel dressing, hydrocolloid dressings changed 1 to 2 times weekly or surgical debridement 1-3 times weekly.15

The healing of the wounds was measured by digital photography looking at the width, length, circumference and surface area. There were four outcomes measured in this study: the amount of necrotic tissue debrided; the amount of granulation tissue observed; the wound surface area differentiations and; the amount of time it took for complete wound healing. Maggot debridement therapy reduced the necrotic surface area by 50% in 9 days. Conventional therapy took 29 days to reach the 50% level which was a statistically significant result (P<0.001). Wounds using maggot therapy were completely debrided by 4 weeks. At 5 weeks with conventional therapy 33% of the necrotic tissue covering the wounds remained (P=0.001). Repeated measures of ANOVA were used to assess MDT efficacy. Within 2 weeks wounds that were treated by MDT showed a significant decrease in necrotic tissue, a mean value of 4.1 cm². When considering granulation growth and healing rates, maggot wounds were covered with 56% healthy tissue after 4 weeks of debridement compared to 15%
coverage of granulation over the wounds treated by conventional therapy (P=0.016). To factor in the wounds that were treated first by conventional therapy and then by maggot therapy, paired t test comparisons were used. The wounds that were treated with maggot therapy were larger in size (~9.7 cm²) and conventional therapy wounds were smaller in size (~3.8 cm²). The authors stated that this did not make a significant statistical difference. There were weekly changes in surface area that were significantly different. Conventional therapy wounds increase 1.0cm²/week in surface area while maggot therapy wounds decreased .9cm2/week (P=0.018). This showed greater wound healing progress in patients using MDT treatment because of the significantly smaller mean surface area.¹⁵

Wolff et al¹⁶ conducted a study that looked at the efficacy of maggot therapy on necrotic or sloughy chronic ulcers. This is an open- retrospective study observing 74 patients over 3 years. The patients ranged in age from 25-94 years old with a mean of 72 years, all of whom had diabetes. This study took place in the County of Vastra Gotaland, Sweden. Each patient had a report done after treatment that included the type of ulcer, necrosis amount, if there was an odor and slough, any indication of pain as measured by the visual analogue scale (VAS) and possible side effects. A picture was taken before and after a treatment. Larvae of *Lucilia sericata* were inserted into the wound using 5-10 larvae/cm². A ring of hydrocolloid dressing was placed on the margins of the wound that was then attached to the Tegapore net that covered the entire wound. After 1-3 days the larvae were removed from the wound.¹⁶

Necrotic tissue in the ulcer was seen in 69 out of 74 patients and 5 out of 74 had fibrin slough. Out of the 69 necrotic ulcers, 59 patients had 66-100% debridement. The remaining ulcers were not complete along with 5 sloughy ulcers, which were considered failures (which the authors attributed to larval death because of the drying out issues). Only one larval application was needed for 53 out of 74, while two treatments were needed for 14 and 3-4 treatments in 7 of the patients. Diabetic patients made up 29 of the participants which all debrided well. Thirty-one patients had odor in the beginning and 18 of them experienced reduced odor after treatment. Using the VAS, 61 patients could describe their pain
experience. Twenty-one had more pain during treatment; 4 had to be stopped because of the intensity of the pain. Fifteen patients experienced a decrease in pain during the treatment which had been worse before the initiation of the maggots. Twenty-five patients experienced no change in the pain level.\textsuperscript{16}

Armstrong et al\textsuperscript{17} observed maggot therapy efficacy in patients in hospice. There were 60 non-ambulatory patients with diabetic foot wounds and a mean age of 72. They had to meet a few criteria in order to participate in the study. These included a prior diagnosis of Diabetes, a patient with a single wound on the foot who requires a wheel chair or some assistive device for movement, a peripheral vascular disease diagnosis, with ischemia or ischemia with infection that is complicating wound healing, and time for at least 6 months of follow up. Thirty patients went through maggot debridement therapy over a period of 3 years. They were compared to 30 patients of similar age and gender that received conventional therapy. This allowed for a 1:1 ratio between patients receiving MDT (case) to patients receiving other wound care treatment (control). Vascular disease status was supported by the absence of more than one foot pulse or non-audible sound on Doppler ultrasound of dorsalis pedis and posterior tibial on affected extremity.\textsuperscript{17}

There were several outcome evaluations that included healing time, amount of infection, and number of days without antibiotics during 6 month follow up. There were no significant differences in age, gender, duration of diabetes, or wound size when comparing the control and case groups. Twenty-seven patients with PVD healed during the 6 month follow up with no significant difference in control vs. MDT group. The MDT group had a faster healing time than the conventional therapy group. The mean time for MDT was 18.5 weeks while the control took 22.4 weeks (P=.04). One in five patients had to have some sort of amputation and that was found to be 3xs more likely to happen in the control group. During the 6 months of follow up, the MDT group had more antibiotic free days 126.8 + 30.3 to 81.9 +42.1 days (P=.0001).\textsuperscript{17}

Dumville et al\textsuperscript{18} performed a larger study comparing the effectiveness of maggot therapy with standard conventional treatments. This study had 267 patients with at least one venous or mixed
venous and arterial ulcer with necrotic or slough tissue. This was a randomized controlled trial held in the United Kingdom from 2004 to 2007 in different medical settings. The main outcomes of the study were time to healing, time to debridement, quality of life and health issues, bacteria and more specifically MRSA, adverse events and pain. The patients were included if they had non-healing ulcers that were ≤5cm². If there were multiple ulcers, the largest ulcer was chosen as the chief lesion. Participants were randomized to receive loose larvae, bagged larvae or hydrogel. Sterile *Lucilia sericata* larvae were used for 3-4 days and nurses could assess the patient’s status and decide whether the time period needed to be different. If more larvae therapy was needed, hydrogel and bandage was used in the intervening time. The control group received a knitted viscose dressing with hydrogel and compression if necessary. The nurse overseeing the patient determined the frequency of application. After the debridement phase was over a viscose dressing was applied either with or without compression. Overall, the maximum length of follow up was 12 months.¹⁸

The time to healing the main ulcer was the primary outcome. Nurses took pictures weekly for 6 months and then once a month for the duration of the study. An ulcer was considered healed once the skin grew a new epithelial covering without a scab. The time to healing showed no significant difference between the groups. The larvae group median healing time was 236 days and the hydrogel group was 245 days. The hazard ratio for healing using larvae versus hydrogel 1.13 (95% confidence interval 0.76 to 1.68; P =0.54). Larval therapy reduced the time to debridement; the hazard ratio with comparison of the larvae group to the hydrogel group was 2.31 (95% CI 1.65 to 3.24, P<0.001). Quality of life and health issues showed no significant difference between the groups. When considering MRSA, 6.7% of the patients were positive at baseline, and there was no difference in eradication of MRSA between the therapies. The mean ulcer related pain scores were higher in both larvae groups compared to hydrogel. When comparing loose larvae (n=82) to hydrogel (n=71) the mean difference was 46.74 (95% CI 32.44 to 61.04, P<0.001). Bagged large vs. hydrogel, the mean difference was 38.58 (95% CI 23.46 to 53.70, P<0.001).¹⁸
DISCUSSION

Study Limitations

There is the lack of articles on this subject because maggot debridement therapy is still a fairly unknown treatment. The limitation of performing a study on maggot therapy is that it is difficult to have double-blinded studies. The patients know what treatment they will receive along which can have an overall effect on the perception of the treatment. The clinical staff also knows what treatment is being used on the patient and this can introduce bias. With these limitations comes studies with too small of sample size to obtain a well-built model of the population.

Research Evidence

In the five studies that were reviewed, there were differences in methodology, sample size, length of study and follow up, types of wounds and conventional treatment.

In the 2002 study performed by Sherman,\textsuperscript{14} it was determined that maggot therapy was efficient in debriding 43 chronic pressure ulcers in comparison to conventional therapy with 49 ulcers. Even though the maggot treated wounds were larger, they were debrided faster, developed granulation tissue during the 5-6 week period and had a higher probability of completely healing. Most of the standardized treatments were conservative rather than surgical debridement. It is difficult to say if MDT is more effective in debridement compared to surgery, but it is clearly superior to conventional therapy. Most patients accepted MDT with few complaints of pain, and adverse events were minimal. The study explained that the maggot treated wounds were initially larger than the conventionally treated wounds and it would be important to know whether that was a coincidence or if it was purposely chosen.

In the 2003 Sherman\textsuperscript{15} study, only 18 diabetic patients with 20 non-healing wounds were studied. The wounds were broken down, 6 wounds treated with conventional therapy, 6 with MDT and
8 with conventional therapy first, and then MDT. Necrotic tissue showed no significant change except when factoring for treatment; MDT treated wounds decreased in size more quickly than conventional therapy. The rate of wound closure with MDT was not significantly superior to wounds using conventional therapy; even though MDT debrided wounds faster which prepared them for closure. Sherman stated that the wounds on patients that were using MDT were larger but did not talk about the reasoning behind that. This study demonstrated overall that MDT is effective in treating wounds that were not responding to conventional therapy.

In the Wolff et al\cite{16} study, patients were being treated by maggots after conventional treatments failed. The purpose was to determine whether maggot therapy is an effective treatment for debriding ulcers. Out of 74 patients, the majority of wounds were debrided after one application. The patients had various types of ulcers and disease entities. This was a problem because it was difficult to compare wound dimensions and healing outcomes. In the end, MDT was effective in debridement. The debridement phase was quick and accurate. The problem with this study was that there was no control group; it simply looked at maggot debridement therapy’s effectiveness with no comparison to other therapies.

In the Armstrong et al\cite{17} study, a different type of population was studied using 60 non-ambulatory patients in which 30 used MDT and 30 were a control group. They discovered that MDT lowers short-term morbidity in people who have diabetic foot wounds and are not mobile. This is not a popular study with many researchers because this focuses on delaying infection along with more aggressive treatments. The determination of PVD was not very strong and left room for error which could have affected the outcomes of certain patients. Patients that used MDT had significantly more antibiotic free days than the patients who used conventional therapy. Although this study was different from most of the other research it shows that maggot therapy helped heal these wounds to a certain extent and the patients with MDT were less likely to undergo surgery or amputation.
In the 2009 Dumville study, patients’ ulcerated wounds were being treated with either maggot therapy or hydrogel. This is the first randomized controlled study exploring the effect of MDT on wound healing. This was one of the largest studies dealing with large numbers of patients. Although many patients did not qualify because they lacked slough, or withdrew due to problems with treatment or lack of follow up. There were several limitations to this study including the lack of follow up on how many ulcers remained debrided in the long term. Another problem was the level of autonomy of the nursing staff in regards to the treatment which could have had an affect on the measured outcomes. Overall, maggots debrided the wound faster than hydrogel. There was no difference in reduction of bacteria and healing times. This was one of the first reports showing that maggot therapy caused more pain. The main outcome showed that maggot therapy significantly reduced the time to debridement of ulcers.

Future Research

It would be beneficial to look into the cost effectiveness of maggot therapy for debridement in comparison to other therapies. To assess when MDT should actually be used and if it should be considered a first line therapy for treating non-healing wounds. Also, many people talk about the psychological problems behind using maggot therapy. A further look into how patients feel and how the clinicians who are performing the treatment are feeling is needed. It remains unclear whether this is an actual issue. The last randomized study discussed pain experienced by some of the patients as one of their outcomes, although not intentionally studied in this paper.18 Another idea to consider would be to look into maggot therapy versus a single standardized treatment. Dumville et al18 compared maggot therapy to hydrogel which was helpful in determining which was more effective. Past studies evaluated maggot therapy in comparison to a variety of treatments that limit our ability to depict ultimate conclusions about the efficacy of MDT. More randomized controlled trials are necessary with larger populations of patients and more specific outcomes. Many of the studies have various sizes and types
of wounds, some say that the largest wound is chosen but give no specification as to why that is happening.

**CONCLUSION**

There is still little research on the effectiveness of maggot therapy in comparison to other treatments. If focusing on debridement, larval therapy seems to be quick and produce good results. Recently, antibiotics, gels and surgery have been used for the treatment of chronic ulcers while maggot debridement therapy was used as a last resort method for wound healing. Antibiotics seem to work for some patients but many do not respond or are resistant to it. Surgery is very invasive and sometimes has a tendency to kill off a portion of the healthy tissue because surgeons have a difficult time differentiating healthy from infected/necrotic tissue. Maggot therapy is able to debride necrotic tissue while leaving healthy tissue behind with fast results while destroying the bacteria unresponsive to antibiotics. This systematic review indicates that there are studies that show the effectiveness of maggot therapy in removing non-healing necrotic tissue and that it can be considered for first line therapy or combined therapy with other conventional treatments.
REFERENCES


### Table 1. Summary of Clinical Trials Reviewed

<table>
<thead>
<tr>
<th>Study</th>
<th>Yr. Published</th>
<th>Patients/ Population</th>
<th>Intervention</th>
<th>Comparison</th>
<th>Outcome(s)</th>
<th>Study type</th>
<th>Comments</th>
</tr>
</thead>
<tbody>
<tr>
<td>Sherman(^a)</td>
<td>2002</td>
<td>103 patients</td>
<td>Maggot therapy</td>
<td>Conventional</td>
<td>Debridement, closure. MDT greater coverage</td>
<td>Cohort study</td>
<td>This was done to wounds that were not responding to conventional care.</td>
</tr>
<tr>
<td>Sherman(^b)</td>
<td>2003</td>
<td>18 patients/ 20 chronic wounds</td>
<td>Maggot therapy</td>
<td>Conventional treatments</td>
<td>MDT rapidly debrided wounds</td>
<td>Retrospective chart review</td>
<td>Larger study needed, Patient’s with less advanced disease</td>
</tr>
<tr>
<td>Wolff et al(^c)</td>
<td>2003</td>
<td>74 patients</td>
<td>Maggot therapy</td>
<td></td>
<td>Successful debridement, decrease in malodor</td>
<td>Open study</td>
<td>No comparison to other treatments, limited study</td>
</tr>
<tr>
<td>Armstrong et al(^d)</td>
<td>2005</td>
<td>60 patients</td>
<td>Maggot therapy</td>
<td>Conventional treatments</td>
<td>Wound closure- MDT more rapid.</td>
<td>Case control study</td>
<td>Larger study needed, different population needed- more active</td>
</tr>
<tr>
<td>Dumville et al(^e)</td>
<td>2009</td>
<td>267 patients</td>
<td>Loose larvae and bagged larvae</td>
<td>Hydrogel</td>
<td>Time to healing, time to debridement</td>
<td>Randomized controlled trial</td>
<td>No long term f/u, unable to do double blind studies, small trial number.</td>
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