Matricaria Chamomile: Prevention of Abdominal Adhesions

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Abstract

One of the medicinal plants that have been widely used is Matricaria Chamomile (MC). Researchers have focused on its possible anti-inflammatory pharmacological mechanisms in the treatment of abdominal adhesions and the constituents of MC that are responsible for its effects. This substance includes several active compounds which are biologically active and have inhibitory effects on inflammation such as apigenin, luteolin and quercetin which are flavonoids. Flavonoids pose their anti-inflammatory effects with different mechanisms. Luteolin holds back nitric oxide (NO) production, prostaglandin E2, cyclooxygenase-2 and the expression of inducible NO synthase (iNOS). Apigenin shows its anti-inflammatory activity by inhibiting the production of proinflammatory cytokines. MC also consists of other components that reinforce the anti-inflammatory actions through other pathways. These mechanisms are in accordance with the authors’ concept that MC can prevent inflammation in postsurgical adhesion.

Keywords: Chamomile, Tissue Adhesions, Inflammation

Introduction:

In ancient Rome and Greece, chamomile was used as a medicinal plant. This plant was named chamomile because of its apple-like smell \(^1\). It is used to treat many conditions such as mastitis, hemorrhoids, rheumatic pain, neuralgia, sciatica, gout, eczema, ulcers, wounds, skin irritations diarrhea rash, poison ivy, conjunctivitis, cracked nipples and chicken pox and is administered for external and internal use \(^2\).
Chamomile has been used widely due to its analgesic, antimicrobial, antispasmodic, anti-inflammatory and sedative effects (3, 4). Chamomile’s tea preparation are aqueous infusion is used in folk medicine. It is a member of the family Compositae (Adteraceae). German chamomile (Matricaria chamomilla) and chamomile (Chamaemelum nobile L.) are the two most famous varieties of chamomile. Marticaria chamomilla (MC) is the most common variant is used for medical reasons. Its flowering parts are used to cure or alleviate many disorders, especially those which involve inflammatory conditions (4). Many chemicals such as essential oils that compounds isolated from MC including polyphenols (flavonoids) have proven the advantages of its traditional use (3). Azulenes and terpenoids such as enyne dicolo ether and chamazulene are the main components of MC (5). Chamazulene, terpenoids and bisabolol have shown anti-inflammatory roles (4). In the neutrophilic granulocytes, chamazulene can suppress leukotriene B4 formation and inhibit lipid peroxidation (6, 7). It can also block the peroxidation of arachidonic acid and thus, reduce the inflammatory mediators derived from it. Quercetin, luteolin and apigenin are demonstrated as the phenolic compounds of MC (8, 9). According to several reports, flavonoids have an important role in the immune system and inflammatory processes. They inhibit enzymes that are activated at some stage in certain inflammatory conditions (8). Luteolin is a subclass of flavonoids which shows anti-inflammatory effects through activating antioxidative enzymes, inhibiting inflammatory substances, suppressing the nuclear factor KappaB pathway and reducing the permeability of the vascular system (10). Also, as a flavone in the MC, apigenin, which is non mutagenic, non toxic with a potential for being an antioxidant, can block the intracellular adhesion molecule-1 up regulation in response to cytokines and suppress the expression of cyclooxygenase-2, and its ability to induce apoptosis (11). Over one million cups of MC tea is consumed per day (12).

Pathophysiology Postsurgical adhesion

Various cell types such as coagulation factors, proteases and cytokines are involved in the complex process of peritoneal repair (13). The adhesion formation process is controlled with series of biochemical events than include inflammation, angiogenesis and tissue repair (14). It seems that the main role of peritoneal healing is played by the fibrinolytic system after the operation. In surgery, immediately after peritoneum injury, bleeding results in increasing vascular permeability with extravasation of fibrinogen-rich fluid from the injured surfaces (14-16). At the same time, the inflammatory cells migrate, cytokines are released and the coagulation cascade activates (13, 16). The latter will cause the formation of thrombin, a substance which is crucial for fibrinogen’s conversion to fibrin (16). This process is a key factor in specifying the amount of adhesion. When fibrinolysis occurs in the first five days after peritoneum injury, the likelihood of peritoneum adhesion to adjacent tissues will decrease (17). On the other hand, if fibrinolysis does not occur in the first seven days, the fibrin matrix will become as a collagen secreting fibroblast and will form the adhesion (13, 18-20). Two major activators exist in the fibrinolytic system; Urokinase like plasminogen activator and tissue plasminogen activator. These two systems help the process of plasminogen conversion into active plasmin, which is a broad range protease that can degrade fibrin (13, 15). Fibrinolysis is stopped with the effects of
plasminogen and thus, adhesion formation is encouraged (15, 21-23). There are other substances that are important in adhesion formation. Inflammatory mediators are one of them. Evidence shows that certain mediators, such as interleukins and transforming growth factors, increase the formation of adhesions through decreasing the fibrinolytic capacity of the peritoneum (24-27).

**Prevention of peritoneal adhesions**

Three strategies have been used in animal models to reduce the formation of adhesion:

1. Changing the fibrinolytic pathway by using gonadotrophin releasing hormone agonist or recombinant t-PA (28, 29).
2. Immunomodulation by using IL-10 and ketorolac (NSAID), transforming growth factor (TGF)- bl antibodies, and TNF-α antibodies (30-32).
3. Disrupting the interaction of cells with the extra cellular matrix (ECM).

**Anti-inflammatory agents**

After tissue injury, the inflammatory response is initiated by anti inflammatory agents. Low dose aspirin may reduce the formation of adhesion by its selective inhibition of thromboxane-A2 over prostacyclin. Rodgers et al demonstrated in their study that retinoic acid, dipyridamole and quinacrine reduce animal adhesions due to their anti inflammatory activities (36). However, these agents have their own complications; delayed wound healing, immunosuppression that follows with wound infection, wound dehiscence and incisional hernia. NSAIDs block the effects of prostaglandins that cause adhesion (37).

As shown in table 1, previous studies have shown the anti inflammatory mechanism of MC.

**Table -1: Main anti inflammatory mechanisms of MC**

<table>
<thead>
<tr>
<th>Mechanism</th>
<th>Compound</th>
<th>Reference</th>
</tr>
</thead>
<tbody>
<tr>
<td>Modulation of NF-κB</td>
<td>Apigenin</td>
<td>Nicholas et al. (2007)</td>
</tr>
<tr>
<td></td>
<td>Luteolin</td>
<td>Chen et al. (2007)</td>
</tr>
<tr>
<td>LTB4 blocker</td>
<td>Chamazulene</td>
<td>Safayhi et al. (1994)</td>
</tr>
<tr>
<td>Antioxidant activity</td>
<td>Apigenin</td>
<td>Lee et al. (2007)</td>
</tr>
<tr>
<td></td>
<td>Luteolin</td>
<td>Seelinger et al. (2008)</td>
</tr>
<tr>
<td></td>
<td>Chamazulene</td>
<td>Rekka et al. (1996)</td>
</tr>
<tr>
<td>Vascular dilation</td>
<td>Luteolin</td>
<td>Seelinger et al. (2008)</td>
</tr>
<tr>
<td></td>
<td>En-yne dicycloether</td>
<td>Miller et al. (1996)</td>
</tr>
<tr>
<td>Gene Supression through the</td>
<td>Apigenin</td>
<td>Nicholas et al. (2007)</td>
</tr>
<tr>
<td>expression of iNOS and COX-2</td>
<td>Luteolin</td>
<td>Chen et al. (2007)</td>
</tr>
</tbody>
</table>
Discussion:

Many literatures support the fact that inflammation plays an important role in initiating pathological events. On the other side, it has been proven that NSAIDs and corticosteroids can manage acute and chronic inflammations. However, these agents have not cured inflammatory conditions, which may be caused by the administration restrictions. These restrictions are due to a number of side effects including peptic ulcer and abdominal pain (38). This shows the necessity to look for other anti inflammatory agents. In this regard, natural products are finding their way and are used worldwide. However, their role in prevention and treating inflammatory conditions has yet to be proved. Many studies have shown good results regarding the anti inflammatory effects of natural productions (39-43). Plant derivatives have been widely used a source for the treatment of acute and chronic inflammation (44, 45). MC is a popular choice that is consumed as herbal teas (3). The flowering parts of this plant has been used internally and externally to decrease the signs and symptoms of inflammatory disorders (4).

The main flavonoids of MC are lutelin, quercetin and apigein (45). Therefore, due to their anti inflammatory effects, MC might be used as a preventive agent in post surgical adhesions. Apigenin suppresses p65 phosphorylation which blocks the expression of proinflammatory cytokines (such as interleukin 1 and 6 and tumor necrosis factor-alpha) and thus inactivates the NF-κB pathway (46). This leads to the regulation of prostaglandin and NO production (47).

In rheumatoid arthritis, there are highly differentiated cells called synovial T cells that express a phenotype that seems to be susceptible to apoptosis (48). Apigenin can induce apoptosis in leukemic cells (49). As a natural antioxidant, luteolin limits the free radicals. It can active antioxidative enzymes, suppresses the NF-κB pathway inhibits pro inflammatory substances, suppresses the production of NO and prostaglandins 2, expresses iNOS, cyclooxygenase-2 (COX-2), TNF-α and IL-6 (10, 50).

Numerous pathophysiological conditions such as postsurgical abdomen inflammation are associated with reactions related to free radicals. The antioxidant activity of chamazulene (the active substance of chamomile) inhibits lipid peroxidation and blocks chemical peroxidation of arachidonic acid which leads to anti inflammatory effects. It also blocks leukotriene B4 formation in neutrophilic granulocytes (6, 7). En-yne dicycloether can prevent histamine release via the degranulation of mast cells and therefore blocks vascular dilation (51).

Based on previous studies, we think that two main anti inflammatory mechanisms can be responsible for MC’s pain relief that is seen in gouty arthritis. The first mechanism is through the antioxidant activity of apigenin, luteolin and chamazulene which prevents the peroxidation of arachidonic acid and therefore blocks the production of inflammatory substances. The other mechanism is that it prevents the activation of NF-κB and suppresses the expression of iNOS and COX-2 gene via apigenin and luteolin. Also, other effects of MC such as vasodilatation inhibitory, induction of apoptosis and inhibition of XO might be important in the expression of anti inflammatory effects of MC in postsurgical adhesion. The
above discussed mechanisms can be presumed to interrupt main inflammation pathways in postsurgical adhesion.

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References:


