

# N-acetylcysteine in dermatology

Mohammad Adil, Syed Suhail Amin, Mohd Mohtashim

Department of Dermatology, Jawaharlal Nehru Medical College, Aligarh Muslim University, Aligarh, Uttar Pradesh, India

## Abstract

N-acetylcysteine is a mucolytic drug which is commonly used as an antidote for acetaminophen toxicity. It is a thiol compound, which acts as a donor of cysteine, leading to replenishment of glutathione and thus acts as an antioxidant. It also has anti-inflammatory effects, alters the levels of neurotransmitters, inhibits proliferation of fibroblasts and keratinocytes and causes vasodilatation. Due to these actions, n-acetylcysteine has found use in several dermatologic conditions in systemic and topical form. The drug has been used as an adjuvant in the management of conditions such as toxic epidermal necrolysis, drug hypersensitivity syndrome, trichotillomania, skin picking disorders and onychotillomania, ichthyoses, contact dermatitis, atopic dermatitis, melasma, pseudoporphyria, connective tissue diseases, wound healing and alopecia. It also has a role in protection from radiation-induced skin damage including photo-ageing, photocarcinogenesis and radiation dermatitis. Most indications in dermatology are supported by case reports, small case series and small trials. Higher quality of evidence is needed for its wider use. The drug is cheap and is generally safe with few adverse effects. Thus a greater role is possible for use of n-acetylcysteine in various skin conditions. This review explores the various uses of n-acetylcysteine in the field of dermatology, the evidence supporting the same, the possible mechanisms of action and the adverse effects of the drug.

## Correspondence:

Dr. Mohammad Adil,  
B-9 Rizvi Apartments,  
Medical Road, Aligarh,  
Uttar Pradesh, India.  
E-mail: dr.mohd.adil@gmail.com

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## Introduction

N-acetylcysteine is a common drug best known as an antidote for acetaminophen toxicity.<sup>1</sup> N-acetylcysteine has commonly been used as a mucolytic agent for many decades now. As greater details of the exact mechanism of action of n-acetylcysteine became available, it was tried in a number of diseases. It has found potential use in various medical fields ranging from neurology and psychiatry to nephrology and pulmonology. It has been used as an adjuvant therapy for the treatment of chronic obstructive pulmonary disease, contrast-induced nephropathy, Alzheimer's disease and human immunodeficiency virus (HIV).<sup>2</sup> These effects are largely based on the free radical scavenging property of n-acetylcysteine. This is achieved by its action as an antioxidant in times of stress due to infections, inflammation and toxins.<sup>3</sup> The present review aims to explore the various

uses of n-acetylcysteine in the field of dermatology. This is the first such review in English literature. For the purpose of this review, we searched PubMed, Google Scholar and Scopus database using the following keywords "n-acetylcysteine in dermatology," n-acetylcysteine in skin disease" and n-acetylcysteine in dermatology." Review articles, original articles and case reports were included in the search.

## Pharmacology

N-acetylcysteine is (2R)-2-acetamido-3-sulfanylpropanoic acid ( $C_5H_9NO_3S$ ), a thiol compound which is an N-acetyl derivative of the endogenous amino acid, L-cysteine. It is a white crystalline powder with a characteristic sour taste and slight acetic odor and is stable at room temperature.<sup>4</sup>

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N-acetylcysteine may be used in oral, intravenous or topical routes. The usual oral dose is 200–400 mg. There is high first pass metabolism and half of the drug is bound to plasma proteins [Table 1].<sup>5</sup> N-acetylcysteine rapidly gets deacetylated to form cysteine. The drug rapidly changes to its oxidized form and into metabolites which accumulate in the body.<sup>6</sup> Formation of disulfides on intravenous administration prolongs its half-life.<sup>7</sup> Topical n-acetylcysteine has a bioavailability of less than 3% and is excreted in the urine after metabolizing in the liver.<sup>8</sup>

### Mechanism of Action

The drug mainly acts via its antioxidant effects. The mechanism of action is via one of the following:

#### Antioxidant action

An overproduction of reactive oxygen species leads to a state of oxidative stress which may cause damage to cellular organelles. To quench these reactive oxygen species, the cell has enzymes such as glutathione peroxidase, catalase and superoxide dismutase and sulf-hydryl compounds, of which glutathione is the most important.<sup>9</sup> Glutathione consists of glutamate, glycine and cysteine, the last amino acid limits its synthesis in times of stress.<sup>9</sup> By acting as a donor of cysteine, n-acetylcysteine causes replenishment of glutathione levels and maintains redox balance in the cells. It is important to note that n-acetylcysteine is superior to direct administration of glutathione or L-cysteine as n-acetylcysteine is less toxic, more water soluble and less susceptible to oxidation.<sup>10</sup> Apart from acting as a precursor to glutathione, n-acetylcysteine has also been shown to scavenge reactive oxygen species directly.<sup>11</sup>

#### Anti-inflammatory action

N-acetylcysteine has been shown to decrease the levels of IL-6 in patients on hemodialysis.<sup>12</sup> It has also been demonstrated that TNF- $\alpha$  and IL-1 $\beta$  is decreased in mice models treated with n-acetylcysteine.<sup>13</sup> N-acetylcysteine inhibits the activation of redox-sensitive nuclear factor-kappa B, which stimulates the expression of pro-inflammatory genes in times of oxidative stress, leading to release of a large amount of inflammatory cytokines.<sup>14</sup>

#### Neurotransmission modulation

Another possible mechanism by which n-acetylcysteine acts is via modulation of neurotransmitters. Cysteine dimerizes

to form cystine which is transported across neurons via the cystine-glutamate antiporter and increases the inhibitory glutamate.<sup>15</sup> In addition, n-acetylcysteine has been demonstrated to alter dopamine levels in neurons.<sup>16</sup>

#### Antiproliferative effects

N-acetylcysteine has been shown to exert an inhibitory effect on NIH3T3 fibroblast cells of mice by reversibly blocking the early or mid G1 phase of the cell cycle. This makes n-acetylcysteine a potential drug for preventing and reversing fibrosis.<sup>17</sup> It also inhibits proliferation of human keratinocyte and has found utility in hyperproliferative diseases.<sup>18</sup>

#### Other actions

N-acetylcysteine also has an important role to play in vasodilatation by facilitating the production of nitric oxide.<sup>3</sup> It also has a role in neutrophil activation and attachment to microbes.<sup>19</sup>

The major mechanisms of action of n-acetylcysteine in various dermatological conditions is illustrated in Figure 1.

### Uses

N-acetylcysteine has been used for dermatological purposes in small trials and case reports [Table 2]. Nevertheless, it offers a safe and exciting option for the treatment of skin conditions. These have been discussed below.

#### Drug reactions

##### Toxic epidermal necrolysis

The beneficial effects of n-acetylcysteine in toxic epidermal necrolysis have been ascribed to its glutathione replenishing property, inhibition of tumor necrosis factor- $\alpha$  and IL-1 (the most prominent cytokines in the pathogenesis of this disease) and blockade of cutaneous lymphocyte antigen that directs the inflammatory cells to the skin.<sup>20</sup> Redondo *et al.* were the first to treat a patient of toxic epidermal necrolysis with S-adenosylmethionine, pentoxifylline and

**Table 1: Pharmacokinetics of oral n-acetylcysteine**

Pharmacokinetic property	Value
Oral dose	200-800 mg
Bioavailability	5%
Peak plasma concentration	0.35-0.40 mg/L (1-2 h)
Volume of distribution	0.33-0.47 L/kg
Terminal half life	>6 h
Excretion	70% (feces), 30% (urine)

MECHANISM OF ACTION OF N-ACETYL-CYSTEINE	
Anti-oxidant action	TEN, DRESS, Skin picking disorder, Onychotillomania, Radiodermatitis, Melanoma prevention, Pseudoporphyria, Wound healing, Acne, Alopecia, Psoriasis
Modulation of neurotransmitters	Trichotillomania, Skin picking disorder, Subacute prurigo, Onychotillomania
Anti-inflammatory action	TEN, DRESS, Atopic dermatitis, Contact Dermatitis, Radiodermatitis, SLE, Wound healing, Acne, Psoriasis
Vasodilatation	Pseudoporphyria, Systemic Sclerosis, Wound healing
Maintenance of epidermal barrier	Atopic dermatitis, Contact dermatitis
Anti-proliferative action	Lamellar ichthyosis, Wound healing, Psoriasis, Systemic Sclerosis

**Figure 1:** Mechanism of action of n-acetylcysteine in various dermatological conditions

**Table 2: Indications of n-acetylcysteine in dermatology and the levels of evidence**

Disease	Level of evidence	Dose and route	Remarks
<b>Drug reactions</b>			
Toxic epidermal necrolysis <sup>20</sup>	4	300 mg/day orally	Conflicting results
Drug reaction with eosinophilia and systemic symptoms <sup>28</sup>	4	150 mg/kg in 1 h (loading) then 100 mg/kg in 16 h intravenously	Useful only as adjunct
<b>Psychodermatoses</b>			
Trichotillomania <sup>30</sup>	2	1200 mg/day orally	Useful only in adults but no effect in children and adolescents
Skin picking disorders <sup>36</sup>	2	1200-3000 mg/day orally	Reduces skin picking but questionable effect on quality of life
Subacute prurigo <sup>37</sup>	4	1200 mg/day orally	Varying levels of improvement seen
Onychotillomania <sup>39</sup>	3	200-800 mg/day orally	Questionable benefit in trial but case reports show clear benefit
<b>Diseases with altered epidermal barrier and abnormal keratinisation</b>			
Ichthyoses <sup>8</sup>	4	10% cream topically	Benefit in lamellar ichthyosis and collodion baby
Atopic dermatitis <sup>44</sup>	3	20% solution topical	Decreases transepidermal water loss and increases hydration
Contact dermatitis <sup>46</sup>	4	10% cream topically	Improvement
<b>Photodermatoses</b>			
Ultra-violet mediated damage of skin <sup>48</sup>	3	1800 mg/day orally	No benefit
Melasma <sup>54</sup>	3	4.7% cream topically	Benefit in combination with 2% hydroquinone
Pseudoporphyria <sup>55</sup>	4	800-1200 mg/day orally	Effective in pseudoporphyria associated with/without renal failure
<b>Connective tissue diseases</b>			
Systemic sclerosis <sup>60</sup>	3	15 mg/kg/h intravenously	Improvement in digital ulcers and Raynaud's phenomenon
Sjogren's syndrome <sup>81</sup>	2	600 mg/day orally	Improvement in halitosis, dry eye and dry mouth
Systemic Lupus Erythematosus <sup>61</sup>	3	1200-4800 mg orally	Improvement in fatigue and SLE disease activity index
<b>Wounds</b>			
Ulcers of bullous morphea <sup>68</sup>	4	10% cream topically	Improvement
Nonhealing ulcers <sup>64</sup>	4	300 mg ampules topically	Improvement
<b>Polycystic ovarian syndrome and hyperandrogenism</b>			
Hirsutism <sup>70</sup>	1	1200-1800 mg/day orally	Improves ovulation but no effect on hirsutism
<b>Acne</b>			
Comedonal acne <sup>72</sup>	3	5% gel topically	Reduction in comedones
Papulopustular acne <sup>71</sup>	2	1200 mg/day orally	Reduction in inflammatory lesion count

Levels of evidence: As per Oxford Centre for Evidence Based Medicine, 2011

n-acetylcysteine.<sup>21</sup> This was followed by another report in two patients who recovered after 300 mg/kg/day of intravenous n-acetylcysteine.<sup>22</sup> Similarly, patients were treated with 600 mg of intravenous n-acetylcysteine administered 8 hourly<sup>23</sup> and 300 mg/kg/day.<sup>20</sup> However, Paquet *et al.* found that n-acetylcysteine alone or in combination with infliximab does not alter the inflammatory cascade of toxic epidermal necrolysis and showed no improvement in overall survival.<sup>24</sup>

#### **Drug reaction with eosinophilia and systemic symptoms**

N-acetylcysteine acts by detoxifying reactive oxygen species produced by the offending drug, which have been implicated in the disease pathogenesis and hence the drug is effective only when given early.<sup>25</sup> Reports of treatment of this disease with n-acetylcysteine alone are conflicting and reviews on the management of this disease do not mention n-acetylcysteine

as a treatment option.<sup>26</sup> Thereafter, n-acetylcysteine was used in conjunction with steroids or intravenous immunoglobulins and found to be a promising option.<sup>27,28</sup>

#### **Psychodermatological conditions**

##### **Trichotillomania**

Trichotillomania is an abnormal habit and impulse control disorder characterized by a sense of tension immediately before pulling hair or when trying to resist pulling and relief of this tension after hair pulling. The mechanism of action of n-acetylcysteine in trichotillomania is believed to be the reduction of glutamate levels in the nucleus accumbens.<sup>29</sup> A double-blind, placebo-controlled trial was conducted on 50 patients of trichotillomania divided into two equal groups. Daily supplementation with 1200–2400 mg/day of n-acetylcysteine for a period of 12 weeks resulted in significant reductions in the severity of hair pulling compared

to placebo.<sup>30</sup> Small case series and case reports also report benefit.<sup>31,32</sup> A randomized double-blind, placebo-controlled trial on 39 children failed to show any benefit of n-acetylcysteine in trichotillomania. The authors concluded that this occurred due to the difference in the pathology of trichotillomania in children where the urge to pull hair is usually absent but hair are pulled as a habit.<sup>33</sup>

#### **Skin picking disorder and prurigo**

Skin picking or dermatotillomania has been classified as a distinct entity different from obsessive compulsive disorders.<sup>34</sup> These effects are due to the antioxidant and glutamate modulatory effects of n-acetylcysteine. N-acetylcysteine has been used in the treatment of skin picking in patients of Prader–Willi syndrome in a small case series.<sup>35</sup> A double-blind, randomized, placebo-controlled trial was conducted on 66 patients of skin picking disorder and n-acetylcysteine (1200–3000 mg/day orally) was found to reduce the urge or craving to pick the skin compared to placebo.<sup>36</sup> There was no statistically significant improvement on the quality of life in patients, which the authors attributed to the small sample size and a relatively short follow-up period of 12 weeks. Varying levels of improvement in the appearance of skin and skin picking was seen in three patients of subacute prurigo who received 1200 mg of n-acetylcysteine orally.<sup>37</sup> However, further studies are needed for patients with skin picking disorder before a final conclusion is drawn about its efficacy.

#### **Onychotillomania**

Nail tic disorders include nail biting or onychotillomania and onychophagia. N-acetylcysteine has been shown to reduce the symptoms of nail biting in case reports due to its effect on glutamate modulation.<sup>38</sup> A double-blind, placebo-controlled trial using oral n-acetylcysteine at a dose of 200–800 mg/day in children and adolescents showed that the nail length in group taking n-acetylcysteine increased significantly more than the nail length of the placebo group after 1 month of treatment, but the length was not significant after 2 months. This disparity may have been due to the continued nail growth prompting some subjects to trim their nails.<sup>39</sup>

#### **Diseases with disturbed epidermal barrier/keratinization disorders**

##### **Ichthyoses**

The effect is due to the anti-proliferative effects of n-acetylcysteine which diminishes the hyperkeratosis of lamellar ichthyosis and improves the skin barrier function.<sup>8</sup> The first article showing improvement of lamellar ichthyosis by topical n-acetylcysteine was published in 1999.<sup>18</sup> Another report from Turkey showed improvement in a collodion baby with 10% n-acetylcysteine oil emulsion applied twice daily over 4% urea in a split body trial.<sup>40</sup> The patient showed complete resolution of eclabium and ectropion by the 16<sup>th</sup> day of treatment. Similar improvements were seen in a 5-patient case series that used 10% n-acetylcysteine in 5% urea emulsion for 4 months.<sup>8</sup> Deffenbacher described a

case with sustained benefit of n-acetylcysteine in a child.<sup>41</sup> An improved formula containing n-acetylcysteine has been proposed to avoid the odor emanating from the oxidation of the n-acetylcysteine cream.<sup>42</sup>

#### **Atopic dermatitis**

Administration of n-acetylcysteine in drinking water to flaky tail mice, the mouse model for atopic dermatitis, led to increased expression of cell adhesion molecules vital for the formation of skin barrier such as epidermal growth factor receptor, E-cadherin, occludin and sirtuin (silent mating type information regulation 2 homolog) 1.<sup>43</sup> A Japanese study based on these findings found that topical 20% n-acetylcysteine for 4 weeks improved the skin hydration and decreased transepidermal water loss in a majority of atopic dermatitis patients as well as healthy individuals.<sup>44</sup> More studies are needed to assess the role of n-acetylcysteine in atopic dermatitis.

#### **Contact dermatitis**

N-acetylcysteine is known to be protective in irritant contact dermatitis and contact hypersensitivity reactions in mouse models which is attributed to its ability to inhibit TNF-alpha by reducing nuclear factor-κB.<sup>45</sup> A case series reported benefit of 10% n-acetylcysteine cream applied to the back of 6 healthy volunteers who were exposed to dimethylsulfoxide.<sup>46</sup>

#### **Photodermatoses**

##### **Protection from photodamage**

A study on healthy adults of lighter skin color showed that n-acetylcysteine cream applied to the skin protected against photoageing by decreasing matrix metalloproteinases in skin.<sup>47</sup> An open-label, randomized study on humans failed to produce a statistically significant protection by N-acetylcysteine in patients of cancer on photodynamic therapy<sup>48</sup> despite animal studies to the contrary.<sup>49</sup> Topical n-acetylcysteine was reported to reduce skin reaction to radiotherapy.<sup>50</sup> Animal studies indicate that n-acetylcysteine may have a role as a prophylactic agent before sun exposure, and thus, may help in the prevention of malignant melanoma as it reduces oxidative stress and decreases the expression of vascular endothelial growth factor in a dose-dependent fashion.<sup>51</sup> It also decreases the expression of Nodal, a gene, whose expression in dysplastic nevi predicts transformation to aggressive melanoma.<sup>52</sup>

#### **Melasma**

N-acetylcysteine acts in melasma probably by increasing glutathione which stimulates the synthesis of pheomelanin, which is lighter in color than melanin.<sup>53</sup> Sulfur in n-acetylcysteine may also complex with copper to inhibit the enzyme tyrosinase.<sup>54</sup> N-acetylcysteine was found to reduce melasma in a double-blind, placebo-controlled study on 12 female patients who were prescribed a combination of 4.7% n-acetylcysteine and 2% hydroquinone. Mild-to-strong bleaching of the skin was observed in 90% patients.<sup>54</sup> No

side-effects due to n-acetylcysteine were noted in any of the patients.

### **Pseudoporphyria**

Most cases of pseudoporphyria occur in renal failure patients on hemodialysis. N-acetylcysteine is proposed to decrease oxidative stress and relieve angiopathy and hypoxia leading to this condition.<sup>55</sup> There are several case reports of the efficacy of this drug in hemodialysis-associated pseudoporphyria.<sup>55,56</sup> Recent case reports also show benefit of n-acetylcysteine in pseudoporphyria patients who were not on hemodialysis.<sup>57</sup>

### **Collagen vascular diseases**

#### **Systemic sclerosis**

N-acetylcysteine has been used in systemic sclerosis due to its effect on vasculature and inhibition of fibroblast proliferation. A one-year, double-blind, placebo-controlled trial, however, failed to show any benefit of n-acetylcysteine (500 mg orally) over placebo.<sup>58</sup> Another study using intravenous infusion of n-acetylcysteine (2 hour infusion of 150 mg/kg, followed by 15 mg/kg/hour for 5 days) resulted in significantly reduced digital ulcers and lower mean recovery time on cold challenge test in 22 patients of systemic sclerosis.<sup>59</sup> These findings were supported by another study on 50 patients of systemic sclerosis and with a mean follow-up of 3 years, which showed decreased attacks of Raynaud's phenomenon and fewer digital ulcers in the patients administered intravenous n-acetylcysteine.<sup>60</sup>

#### **Systemic lupus erythematosus**

Patients with systemic lupus erythematosus have low levels of glutathione in their T cells, predisposing them to pro-inflammatory cell death and necrosis. Glutathione regulates T-cell function via mammalian target of Rapamycin pathway. N-acetylcysteine blocks the mammalian target of Rapamycin pathway in T lymphocytes and improves lupus erythematosus.<sup>61</sup> Oral n-acetylcysteine improved fatigue and systemic lupus erythematosus disease activity index in 36 patients in a double-blind, placebo-controlled trial.<sup>61</sup> N-acetylcysteine has proven to be effective in systemic lupus erythematosus-induced nephritis in a case report<sup>62</sup> and neuropsychiatric conditions in a placebo-controlled, randomized trial.<sup>63</sup>

### **Wound healing**

The effects of n-acetylcysteine on wound healing are related to its action as an antioxidant, support of nitric oxide system, stimulation of cell proliferation, migration and collagenous expression of matrix metalloproteinases.<sup>64</sup> Experimental studies done mostly in animals have reported that n-acetylcysteine is effective in various types of wounds such as burns,<sup>65</sup> incisional wounds<sup>66</sup> and wounds after radiotherapy.<sup>67</sup> Recently, there was a report of healing of non-healing pressure ulcers in two patients with n-acetylcysteine topically applied to the wounds.<sup>64</sup> Ulcers caused by bullous morphea

were treated in a patient with n-acetylcysteine and topical wound care.<sup>68</sup>

### **Polycystic ovarian syndrome and hyperandrogenism**

N-acetylcysteine is proposed to benefit in polycystic ovarian syndrome by lowering insulin secretion and restoring the deranged hormonal profile in affected patients. In an open-label trial, 100 patients were randomized to receive metformin or 1800 mg daily of n-acetylcysteine for 24 weeks. N-acetylcysteine produced significant reduction in free testosterone and hirsutism scores at 6 months after treatment and the results were comparable to the effect produced by metformin.<sup>69</sup> Though n-acetylcysteine has been used in patients of polycystic ovarian syndrome and resulting hyperandrogenism in several clinical trials, a recent meta-analysis of eight clinical trials has shown that acne and hirsutism do not improve significantly when compared with placebo.<sup>70</sup>

### **Acne**

While n-acetylcysteine helps improve inflammatory lesions of acne by quenching reactive oxygen species, inhibition of leukotrienes and prostaglandins, stabilization of membranes and inhibiting lipid peroxidation,<sup>71</sup> its effect on comedones is less well defined and could be due to decreased sebum production or inhibition of *Pityrosporum ovale*, a potential comedogenic organism that has been demonstrated in comedones.<sup>72</sup> A randomized, single-blind trial from Iraq showed that the number of inflammatory lesions decreased significantly in 14 patients who received 1200 mg/day of n-acetylcysteine compared to placebo.<sup>71</sup> Another double-blind, placebo-controlled trial found that the test group comprising 65 patients who received 5% n-acetylcysteine gel for 8 weeks had significantly reduced the number of comedones compared to patients in the control group (34 patients) who received only placebo.<sup>72</sup>

### **Other potential uses**

The role of n-acetylcysteine in androgenetic alopecia is proposed as it has been shown to reduce the free radicals and decrease the senescence of balding human dermal papillae obtained from patients of androgenetic alopecia.<sup>73</sup> Animal studies show that n-acetylcysteine may also help in preventing chemotherapy-induced alopecia.<sup>74</sup> Reactive oxygen species play a role in the tumor necrosis factor- $\alpha$  induced inflammatory pathways in human keratinocytes. n-acetylcysteine, being an antioxidant, was found to play a role in the suppression of this pathway.<sup>75</sup> This finding paves the way for further studies on the role of n-acetylcysteine in psoriasis. While *in-vitro* studies supported the idea that n-acetylcysteine may be useful in the treatment of methemoglobinemia, a crossover, randomized trial on human volunteers with induced methemoglobinemia demonstrated that intravenous n-acetylcysteine offers no reduction in methemoglobin concentration in blood.<sup>76</sup>

## Adverse Effects

N-acetylcysteine is usually safe when administered orally in the dose of 2400 mg/day or lower.<sup>3</sup> The drug has a strong, disagreeable flavor and it needs to be taken with fruit juice or soft drink for this reason.<sup>10</sup> Side-effects at this dose are mild and include nausea, vomiting, diarrhea, flushing, pain in the epigastric region, constipation and skin rash. At higher dosage, urticaria, chills, skin rash, headache, tinnitus and fever may be seen.<sup>10</sup> The frequency of side-effects with oral administration of the drug is at least as much as that of intravenous administration.<sup>77</sup> Intravenous administration of the drug may lead to an anaphylactoid reaction, which may present as urticarial rash, pruritus, angioedema, bronchospasm and hypotension. Females and those with atopic diathesis are more prone to develop this type of reaction, which is supposedly produced by non-immunological mechanism under the influence of histamine.<sup>78</sup> N-acetylcysteine may also destabilize the disulfide bonds in clotting factors and modestly prolong the International Normalized Ratio, though this may not be clinically significant.<sup>79</sup> Topical use of n-acetylcysteine is generally safe and may be associated with mild side-effects such as burning, erythema and pruritus.<sup>41</sup>

N-acetylcysteine should be avoided in patients taking nitroglycerin or related medications as this may cause hypotension by vasodilatory effects and by reversing the tolerance to nitrates.<sup>80</sup> Use of n-acetylcysteine in pregnancy is not indicated unless absolutely necessary due to the dearth of studies in pregnant women. Excretion of the drug in breast milk or its crossing the placental barrier in pregnancy is controversial and animal studies have shown doubtful embryotoxicity.<sup>5</sup>

## Conclusion

Though an old drug, the potential of n-acetylcysteine has probably not been fully recognized in dermatology. It is a relatively safe drug, and can be used intravenously, orally and topically. The effects of n-acetylcysteine are largely based on its antioxidant and anti-inflammatory properties and its modulation of neurotransmitters. However, the studies evaluating its efficacy are few and small and have shown only modest benefit. More controlled human studies are needed to confirm its efficacy in various skin diseases. Furthermore, correct dosage regimens need to be established for the optimal utilization of this drug in various dermatological conditions.

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## Conflicts of interest

There are no conflicts of interest.

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