A New Approach for the Topical Treatment of Acne Vulgaris by Clindamycin HCl Supported on Kaolin

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Abstract:

Background: the treatment of acne vulgaris should act against hyperkeratinization, inflammation, bacterial proliferation and sebum production. At the present, there is no topical anti-acne medication that acts against all of the above pathophysiologic features of acne. The acne vulgaris response to the clindamycin is better than other available antibiotics. Kaolin by itself can be useful in sorption of bacteria, pus, toxins and free fatty acids.

Aim of the study: The aim of this work is to study the role of the adsorption – desorption process in prolonging the action of the clindamycin drug .

Patients and Methods: adsorption of clindamycin HCl from 70% ethanol solution on different amounts of kaolin as adsorbent was studied using UV-spectrophotometry technique at 210nm. Desorption process of the adsorbed clindamycin HCl from kaolin surface was also studied.

Results: A stable formula consisting kaolin, clindamycin HCl and 70% ethanol aqueous solution has been prepared for the treatment of acne vulgaris.

Conclusion: The formula provides prolonged action accompanied with a certain mechanism of clindamycin adsorbed on kaolin upon application on the skin leading to fairly good results in the treatment of acne vulgaris. The mechanism of action of the formula is based on the adsorption-desorption processes of the antibiotic on the clay. *Keywords:* Clindamycin; kaolin; adsorption; acne vulgaris

Introduction:

A large number of people of all over the world especially teenagers are suffering from acne vulgaris. It is a chronic inflammatory condition, in which excessive sebum secreted by over active sebaceous glands is unable to escape from the hair follicles [1]. The increase and abnormal keratinization at the exit of pilosebacious follicles obstructs the flow of sebum; this state will let the bacteria, propionobacterium acne, to play a pathogenic role. propionobacterium acne is a normal skin commensal; it colonizes the pilosebaceous ducts, breakdown the triglycerides releasing free fatty acids, produces substances chemotactic for inflammatory cells and induces the ductal epithelium to secrete pro-inflammatory cytokines [2]. Hence, the treatment of acne vulgaris should act against hyperkeratinization, inflammation, bacterial proliferation and sebum production. At present, there is no topical anti- acne medication that acts against all of the above pathophysiologic features of acne [3]. The combination of two or more medications may be necessary to

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integrate the effect of the drugs towards acne features. Many preparations containing clindamycin as an antibiotic tom act against Gram positive cocci anaerobic [4] have been prescribed and used topically [5-8].

The use of antibiotics alone is associated with the problem of resistant strains of propionobacterium acne [9, 10]. However, the p-acne response to the clindamycin is better than other available antibiotics [11-13]. The main mechanism of action of topical antibiotics for acne treatment is the inhibition of inflammation caused by bacteria rather than a direct bactericidal effect [14].

Kaolin is widely used as adsorbent of many substances including drugs [15-16], bacteria and their toxins [17]. Iraqi kaolin was investigated in previous studies [18-19] for its adsorption ability of some drugs. The clay was found of appreciable surface activity and exhibiting a good adsorption capacity for many drugs. In traditional medicine, kaolin has been used for multiple purposes, particularly, in the treatment of acne vulgaris and for removal of hair dandruff.

In this work, an attempt was made for the preparation of a new formula containing a mixture of the antibiotic, clindamycin, in 70% v/v ethanol aqueous solution and kaolin clay as a surface active adsorbent. Kaolin is expected to play a significant role as an adsorbent for bacteria and sebum as well as its possible function as a clindamycin adsorbent which may result in gradual and prolonged contact of the drug with the skin through the adsorption process.

Experimental

A- Materials:

Pure clindamycin (B.P.) obtained from the Arab Company for Antibiotic Industries (ACAI). Ethanol 99% v/v obtained from BDH and the kaolin from Dwaikhla mine supplied by the (Iraqi General Company for Geological Survey and Mining). Analysis of kaolin has shown the following w/w% composition: SiO_2=54.68, Al_2O_3=30.19, Fe_2O_3=1.02, TiO_2=1.00 and the loss on ignition =10.94.

B-Methods

In all experiments, pure clindamycin was brought into solution using 70% v/v ethanol aqueous solution as a solvent. Kaolin samples were prepared by washing the clay with distilled water followed by 70% ethanol aqueous solution. The clay was then dried at the 160°C for three hours, grinded to 75μm and kept in tight container.

A volume of 5ml of eight different initial concentrations (C_o) in the range 3-10 g/L of pure clindamycin HCl solution was added to 500 mg of the kaolin adsorbent in test tubes supplied with tight covers. The contents of each tube were vortexed and incubated at 25C for one hour (the time required to reach equilibrium that determined in independent experiments and found not to exceed one hour) and then centrifuged at 3000 rpm for 15 minutes. Clindamycin HCl equilibrium concentration in each tube (C_e) was estimated spectrophotometrically in the UV-region using a (UV/VIS Pye-Unicam PU-8600 spectrophotometer) at the wave length (λ=210 nm.) of maximum absorbance. Calibration was done in the usual manner by making the appropriate dilution to fit Beer-Lambert law.

The above procedure enables us to study the adsorption isotherms of clindamycin on kaolin system. The reverse process (desorption of the drug from the solid adsorbent) is carried out by isolating the residues obtained from the adsorption experiments followed by 5ml addition of 70% aqueous ethanol to each residue . The samples

were vortexed for two minutes and then incubated at 25°C for 1 hour. Clindamycin HCl that has desorbed to the solution was determined spectrophotometrically as described previously.

A calibration experiments were carried out to check the stability of clindamycin in the slurry. Briefly, twenty tubes that each of them contains the mixture of 5ml of 1% w/v alcoholic clindamycin HCl solution and 0.5g of kaolin was prepared, closed and stored at 25°C. The measurement of the clindamycin concentration in solutions was carried out after 1, 2, 3, 24, 48, and 72 hours then measured twice a week up to 44days.

The effect of the weight of kaolin on the quantity adsorbed was studied using a constant drug concentration (1%w/v alcoholic clindamycin HCl solution) and different weights of kaolin. The procedure of the adsorption also carried out as previously mentioned.

Results and Discussion:

Adsorption isotherm of clindamycin HCl from ethanol aqueous solution on kaolin samples at 25°C is given in Figure (1) where the quantities adsorbed (Q_e) are plotted as a function of clindamycin equilibrium concentration (C_e) at the given temperature of study. Clindamycin uptake by kaolin was found to obey Freundlich adsorption isotherm as confirmed by the linear relationship of (log Q) versus (log C_e) as shown in Figure (2). Freundlich isotherm is expressed by the equation ($Q=kC_e^{1/n}$) which demonstrates the heterogeneity of kaolin surface. From Figure (2) the estimated k and (1/n) values were (0.07) and (1.06) respectively, where k is the capacity of adsorption and (1/n) represents the strength of adsorption. The shape of the adsorption isotherm appeared matching (S3) type according to Giles classification [20].

The water content of aqueous ethanol as a solvent can play a significant role in clindamycin adsorption on kaolin. Adsorption uptake is inversely proportional to the solubility of adsorbate in the solvent [21]. Therefore, the lower solubility of clindamycin in 70% ethanol aqueous solution than in pure ethanol will enhance the clindamycin uptake by kaolin surface leading to higher adsorption capacity. The heterogeneity of kaolin surface reflects a variety of adsorption bond strength in adsorbent-adsorbate system due to fluctuation in potential energies of adsorption sites of kaolin surface [22]. This fact can be demonstrated via desertion process of clindamycin. Kaolin samples that have already adsorbed clindamycin at the temperature of study were subjected to the desorption process as demonstrated in the methodology.

Figure (3) showed a graphical representation of clindamycin desorption from kaolin surface to the solvent phase at the temperature of study. Almost 60% of the adsorbed drug molecules was desorbed indicating the heterogeneity of the surface and the ease of desorption of weakly bound adsorbate molecules. The results showed a slight dependence on the initial drug concentration which could be attributed to the fact that the adsorption from dilute drug concentration may involve a solvent competitive mechanism i.e., the solvent molecules can interact with the adsorbed solute molecules. Consequently, removal of clindamycin from the surface is facilitated particularly, by the weakly bound molecules to the surface.

The suspension of clindamycin and kaolin showed a relatively short equilibrium time (less than 1 hour) accompanied with a good stability of the suspension up to 44

days (Figure 4). Algra *et al* (1977) [22] have reported a stability of six months for the clindamycin HCl formulation containing alcohol and water. In the present work, kaolin appeared not to affect the stability of clindamycin formulation reflecting the inert chemical properties of the clay. Thus, the formula (clindamycin + aqueous ethanol + kaolin) in fairly stable, easy to be prepared and stored for a reasonable period of time.

The mode of action of this formula may be interpreted by slower evaporation of the solvent after application to the skin due to the clay-solvent-solute interactions giving rise to a prolonged contact of the antibiotic with the skin. Moreover, clindamycin is likely to be gradually desorbed from the surface by the thermal energy supplied to the adsorption system by the normal human body temperature.

In the course of inflammation, the skin will excrete sweating and sebum. Probable sorption (adsorption and absorption) of sweating and sebum on the clay surface might occur through an exchange mechanism between the originally adsorbed drug and these materials. This process can allow prolonged action of the drug on the bacteria. Furthermore, kaolin by itself possesses ability in adsorbing bacteria and their toxins [17, 23]. Therefore, the dead skin cells, pus and bacteria could be adsorbed by the clay. Additional function of kaolin in the treatment of acne vulgaris has been reported by Kirby and John [1]; the rough surface of the clay which by rubbing on the skin when it is applied can open the closed comedons and prevent subsequent inflammation.

Figure (5) showed the effect of different weights of kaolin clay on the quantity of drug adsorbed. The results indicated that, the increase in the quantity of drug adsorbed with increasing kaolin amount in the suspension is not linear. i.e. at high amount of adsorbent, the quantity of drug adsorbed was not steadily increased. This reflects the fact that the adsorption is an equilibrium process and the solvent should contain certain amount of dissolved drug molecules in order to obtain equilibrium between the dissolved and the adsorbed drug molecules.

In order to examine the validity and the effectivness of this approach, it has been applied to a large number of volunteers and the results was very satis factory.

This undergoing study, which is carried out under the supervision of a senior dermatologist, trying to improve the effect of this approach still further to satisfy the necessary clinical requirements.

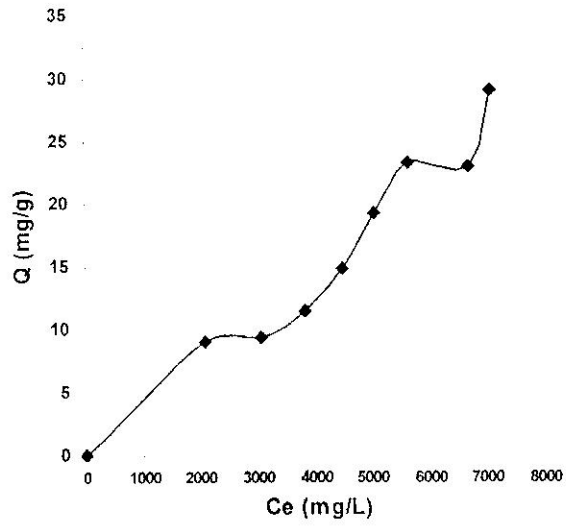

Figure (1): Adsorption isotherm of Clindamycin HCl on Kaolin clay from 70% v/v ethanol aqueous solution.

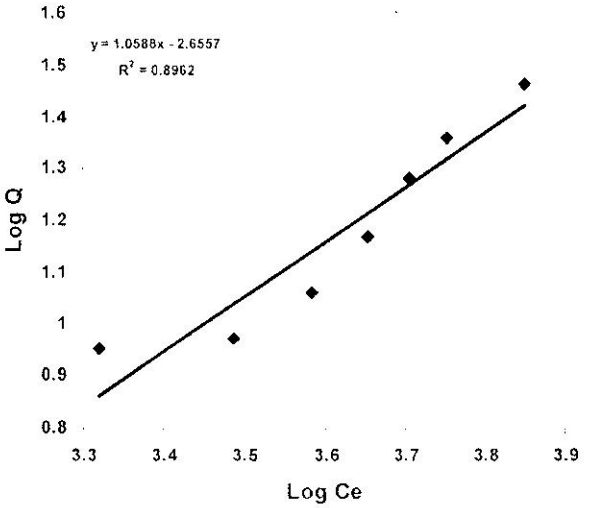

Figure (2): Linear form of Freundlich adsorption isotherm of clindamycin HCl on kaolin.

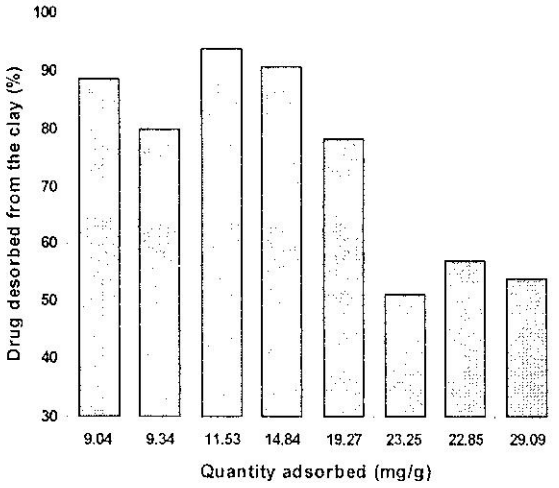

Figure (3): The percentage of the quantity of drug that desorbed from the quantity previously adsorbed on kaolin surface.

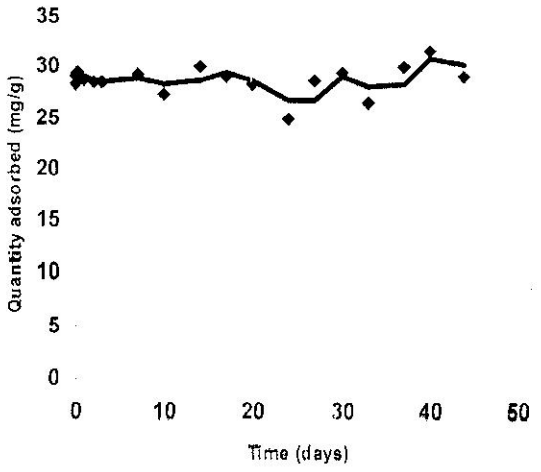

Figure (4): Stability of the quantity of the drug adsorbed on kaolin with time.

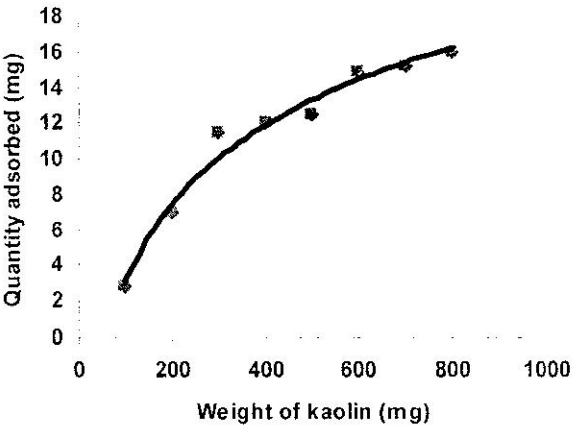

Figure (5): The effect of different weights of kaolin clay on the quantity of drug adsorbed.

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طريقة جديدة للعلاج الموضعي لحب الشباب باستعمال الكلندامايسين هيدروكلورايد المحمول على الكاؤلين

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الخلاصة:

لقد تمت دراسة كل من عمليتي الامتزاز والابتزاز لمادة الكلندا مايسين على كميات مختلفة من الكاؤولين في محلول ٧٠% كحول باستعمال طريقة U.V.Spectroscopy عند الطول الموجي 210nm .

تم تحضير صيغة مستقرة لمزيج الكاؤولين والكلندا مايسين في المحلول الكحولي ٧٠% لعلاج حب الشباب .

تبين ان الصيغة المحضرة للمزيج المذكور توفر اطالة لزمن فعالية الكلندا مايسين الممتز على الكاؤولين عند استعماله على الجلد مؤدية الى نتائج جيدة في معالجة حب الشباب . ان ميكانيكية تاثير هذه الصيغة مبينة على اساس عمليتي الامتزاز والابتزاز للمضاد الحيوي على سطح الكاؤولين .