Effects of Pharmaceutical Excipients on the *in Vitro* Release Rate of Sodium Salicylate from Oily Vehicles

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Abstract

Objectives: The work objective was to study the possible effects of different pharmaceutical excipients on the release of sodium salicylate from oily vehicles.

Methods: Several formulations of Fractionated Coconut Oil (FCO) containing different pharmaceutical additives were prepared. The release rate behaviour of sodium salicylate from these oily formulations was investigated using a dialysis method. The time required for 30% and 50% of the salicylate to appear in solution outside the dialysis sac ($t_{30\%}$ and $t_{50\%}$), respectively, were used as indices for estimating the release rate.

Results: The results of this study showed that the aluminium stearate retards the release rate of salicylate specially when its concentration is 1.5%w/v or more. Oily formulation containing 0.5% w/v aluminium stearate +0.7%w/v lecithin + 0.35% w/v hydrogenated castor oil + 20% w/v sucrose in FCO and oily formulation containing 0.5% w/v Cab-o-sil + 20%w/v sucrose in FCO delayed the release rate of the drug. However, the inclusion of sucrose in the formulations complicates the situation and enhances the release rate especially at the later stages. The enhancing effect of sucrose on the release rate is nullified by the inclusion of 1% w/v Cab-o-sil. Possible reasons for these effects are discussed with particular reference to the tendency forming globules of sucrose, due to the osmotic effect inside the dialysis sac.

Conclusion: Oily formulations (0.5% w/v aluminium stearate + 0.7%w/v lecithin + 0.35% w/v hydrogenated castor oil + 20% w/v sucrose in FCO) and (0.5% w/v Cab-o-sil + 20%w/v sucrose in FCO) can be used as a depot preparations for chronic disease conditions. The enhancing effect of sucrose on the release rate of salicylate can be beneficial if acute response is required. Extrapolation of this study on tablets, capsules and i.m. injection formulations is suggested.

Keywords: Release rate, Oily vehicle, Pharmaceutical additives, fractionated coconut oil.

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Introduction

The *in vivo* methods of assessment of drug bioavailability are expensive and time-consuming. Consequently, many attempts have been made to develop relatively rapid, inexpensive and reproducible methods that can be used either in the development of new dosage forms or in the quality control of existing products. These attempts have usually been concerned with the development and use of *in vitro* models that simulate and describe the dissolution and absorption of drugs *in vivo*. Such models have allowed many useful studies to be carried out on the effects of a variety of factors that are important in the design and control of drug properties.

The development and use of *in vitro* models to discriminate between different formulations and to predict the availability of drugs in particular dosage forms is important when physiological functions play no significant part in regard to this aspect. As no apparatus or procedure can exactly duplicate *in vivo* conditions, all dissolution studies are relative, and the most important considerations are the ones of reproducibility, practicality and reasonableness. However, in spite of this limitation, *in vitro* models still serve as a secondary standards for the detection of the differences in the release of drugs from different dosage forms, and the effect of different pharmaceutical additives.

Dissolution and release rate studies on drugs from different dosage forms have been widely reported and reviewed. However, these reports and studies have concentrated on tablets and capsules, [1-6] and on solutions and suspensions. [7-9] The later studies were devoted to aqueous vehicles but the release rate studies on drugs from non-aqueous vehicles have received little attention. [10, 11] The later studies were done on nitrofurantoin [10] and ampicillin. [11] The study on *in vitro* release rate of salicylate from oily formulations is virtually not existed.

The present work is concerned with the studies of the release rate of sodium salicylate from different oily formulations, compared to aqueous vehicles, in an attempt to detect the possible effects of different pharmaceutical additives on the release characteristics of salicylate.

Materials and Methods

Materials: Sodium salicylate, colloidal silica (Cab-o-sil) and lecithin 90% (refined grade) were obtained from BDH Chemicals (Leicester, England). Fractionated Coconut Oil (FCO) was obtained from Alembic Products Ltd (Chester, England). Aluminium mono and distearate were obtained from Witco Chemical Ltd (USA) and hydrogenated castor oil was obtained from Akzo Chemie U.K. Ltd. And Sucrose (Icing sugar) was obtained from the British Sugar Corporation Ltd (UK).

Preparation of the Vehicles: In addition to a 4% suspension of sodium salicylate in FCO alone (O) and a 4% of the salicylate in distilled water (A), the release rate studies were carried out on sodium salicylate suspensions of the same concentration in the following types of oily vehicles:

Type 1 Vehicles

Aluminium stearate (50:50 mixture of mono and di-stearate) in the following concentrations in FCO were prepared:

A=0.5% w/v, B=1% w/v, C=1.5% w/v, D=2% w/v, E=2.5% w/v, F=3% w/v, G=3.5% w/v, H=4% w/v, I=5% w/v.

Type 2 Vehicles

Related to the formulation of Stephens and Su. [12]

A =0.7% w/v lecithin in FCO
B =0.35% w/v hydrogenated castor oil in FCO
C =0.5% w/v aluminium stearate + 0.7% w/v lecithin + 0.35% w/v hydrogenated castor oil + 20% w/v sucrose in FCO.

D= 0.5% w/v aluminium stearate + 0.35% w/v hydrogenated castor oil + 20% w/v sucrose in FCO.

Type 3 Vehicles

Related to the vehicle of Lin and Pramoda. [13]

A = 20% w/v sucrose in FCO
B = 0.3% w/v Cab-o-sil + 20% w/v sucrose in FCO
C = 0.5% w/v Cab-o-sil + 20% w/v sucrose in FCO
D = 1% w/v Cab-o-sil + 20% w/v sucrose in FCO

Dialysis Method

The dialysis method and apparatus used in this study was based on that described by Barzegar- Jalali and Richards [9] with minor modifications. One end of a 25-cm- length of Visking dialysis tubing (Scientific Instrument Center, Ltd.), having an inflated diameter of 2.14 cm, was tied off after the tubing had been soaked in HCL (0.1 mole/L) for at least 12 hr. Seventy glass beads with an approximate diameter of 3 mm were placed in the tube. These beads regulated the oscillations of the dialysis sac and markedly improved the reproducibility of the results obtained for aqueous suspensions. [9] Five ml of a suspension were poured into the sac and that part of the sac above the level of its contents was flattened between the fingers. The sac was then suspended through the central neck of a 2 L two-necked round-bottomed flask, which contained 1495 ml of 0.1 mole/L HCL, and that was secured by a glass stopper in such a way that the surface of the contents of the sac was 1 ml below the surface of the dissolution medium. Use of these volumes allowed the sink condition to be maintained because the solubility of sodium salicylate in 0.1 mole/L HCL, as determined by prior experiments, is 306.1 mg/100 ml. A thermometer and a glass tube connected to a flexible plastic tube were inserted through a rubber stopper in the side neck of the flask and into the dialysis medium.

The plastic tubing facilitated sampling whilst the flask was shaken. The whole assembly was clamped in a shaking water bath (Gallenkamp) maintained at 37^0C ± 0.1^0C and adjusted to provide an oscillation frequency of 120 ± 2 cycles /min. At this frequency, not only was the dialysis medium well agitated but also the sac was oscillated in a constant manner, thus ensuring good mixing on either side of the membrane. Preliminary experiments showed that this frequency was low enough to discriminate between the release rates of the different formulations. A diagram of the dialysis apparatus is given in Figure (1).

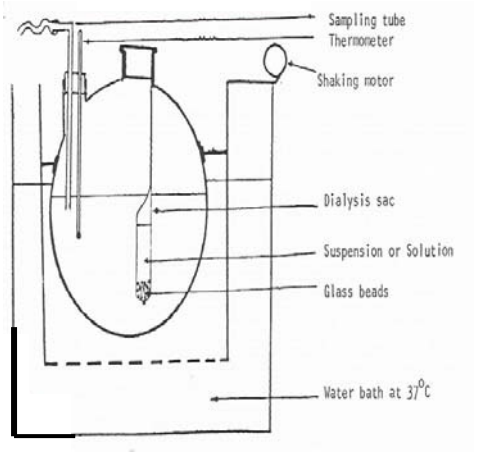

Fig. 1: Dialysis apparatus used for the studies on the rate of release sodium salicylate from aqueous solution and oily suspensions.

Five ml samples were taken from the flask at various times and immediately replaced by the same volumes of 0.1 mole/L HCL. The samples were filtered through a Millipore filter assembly (0.45 µm pore size). The absorbance of the solution was determined using an SP 500 Unicam spectrophotometer at 300.5 nm with 0.1 mole/L HCL as the reference solution.

Spectrophotometric Analysis

The spectrophotometric analysis of all salicylate samples in 0.1 mole/L HCL were performed at 300.5 nm (UV/Visible spectrophotometer, SP 500 Unicam). Standard curves were constructed by serially diluting an aqueous stock solution of the drug (0.1 mole/L HCL) to obtain concentrations in the range of (0.5 – 5 mg/100ml). Each sample was analyzed in triplicate.

Results

The amount of salicylate released, expressed as a percentage of the total amount originally added to the system, was calculated from the drug concentration in each sample and plotted against the sampling time to give a dialysis, or release rate curve. The mean values of these percentages for each formulation are shown in Table (1). Each value is the mean obtained from 3 experiments. The release rate curves for these values are shown in Figures 2- 4. Figure 2 shows the lower and higher concentrations of aluminium stearate, i.e. 0.5% w/v and 5% w/v. All the other concentrations lie between these two curves but have been omitted from the figure for the sake of clarity.

Table 1: Percent [(a)] salicylate released at various times from different formulations using the dialysis method. Each value is the mean of 3 experiments± SD.

Formul[n] (b)	*Time (min)*						
	5	***10***	***20***	***30***	***45***	***60***	***90***
O	*13.2±3.9*	*19.2±3.5*	*27.8±4.7*	*35.2±4.7*	*40.6±4.1*	*43.9±3.8*	*48.6±4.9*
A	*19.2±3.7*	*25.6±5.1*	*36.8±4.3*	*49.3±5.4*	*68.4±5.8*	*85.8±5.9*	*98.5±6.1*
1A	*10.8±3.7*	*17.4±3.9*	*24.3±4.6*	*28.1±5.3*	*32.8±4.6*	*36.0±3.3*	*40.8±4.7*
1B	*10.4±3.2*	*17.0±4.9*	*22.8±4.3*	*27.5±4.9*	*32.2±5.1*	*35.8±5.3*	*40.4±5.1*
1C	*9.0±2.2*	*14.4±4.5*	*20.6±5.3*	*25.8±2.2*	*29.0±5.3*	*31.9±4.7*	*36.8±4.1*
1D	*8.4±3.8*	*13.7±5.0*	*19.4±5.4*	*23.6±4.7*	*27.9±4.8*	*32.9±6.3*	*36.0±5.3*
1E	*7.5±3.1*	*12.7±4.5*	*18.7±5.1*	*23.9±3.9*	*28.9±4.4*	*31.7±5.2*	*35.7±5.4*
1F	*6.1±2.9*	*10.8±4.3*	*17.3±3.9*	*22.3±5.2*	*27.1±5.8*	*30.4±4.9*	*34.9±5.6*
1G	*5.0±2.8*	*9.0±3.7*	*15.2±5.4*	*19.9±2.2*	*24.1±4.7*	*26.4±5.8*	*30.1±6.2*
1H	*5.5±2.2*	*8.8±3.9*	*14.6±4.7*	*18.1±4.6*	*21.2±5.7*	*23.9±4.4*	*28.7±4.3*
1I	*3.4±2.4*	*8.2±3.8*	*14.0±4.5*	*17.8±4.5*	*21.6±4.9*	*24.1±4.7*	*28.1±5.1*
2A	*13.0±4.6*	*18.8±5.1*	*27.4±5.5*	*35.0±3.8*	*40.0±2.9*	*43.4±5.4*	*47.7±4.9*
2B	*11.8±4.2*	*19.5±5.6*	*28.0±4.9*	*34.7±5.9*	*39.2±6.6*	*42.2±5.7*	*46.9±5.8*
2C	*5.4±2.9*	*9.3±3.2*	*15.9±6.2*	*22.3±5.7*	*31.9±5.4*	*40.9±5.6*	*56.8±5.9*
2D	*7.3±2.3*	*11.9±4.1*	*18.3±3.7*	*24.4±5.9*	*32.2±6.3*	*38.5±5.4*	*51.0±5.6*
3A	*7.9±3.7*	*11.7±4.6*	*19.2±5.3*	*26.6±5.1*	*34.7±5.7*	*43.3±4.8*	*56.3±4.6*
3B	*6.9±3.3*	*11.0±3.2*	*19.4±4.3*	*26.6±5.6*	*35.9±5.9*	*44.4±5.1*	*58.9±5.1*
3C	*6.6±2.1*	*10.3±4.6*	*17.6±4.7*	*24.5±5.3*	*34.1±5.4*	*43.5±6.3*	*55.6± 6.7*
3D	*5.6±2.4*	*9.3±3.2*	*15.8±2.9*	*21.5±4.7*	*30.1±4.3*	*38.1±4.1*	*48.5±5.3*

A. Each value is the average of the results from three experiments.

B. Key to formulations: O=simple suspension in FCO, A=aqueous solution, Type 1 vehicles (A-I) contain various concentrations of aluminium stearate in FCO, Type 2 (A-D) and Type 3 (A-D) vehicles are based on those of Stephens and Su [12] and Lin and Pramoda, [13] respectively. Further details are given in dialysis method section.

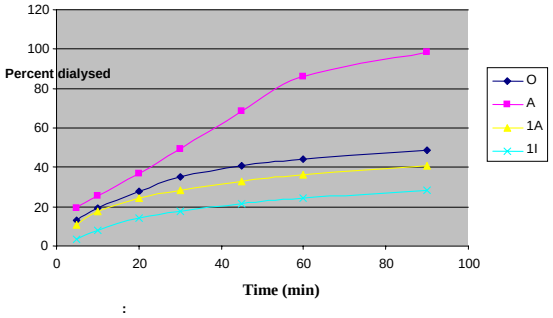

Figure 2: Plot of the percent of salicylate appearing in the dialysis medium versus time for simple oily suspension (O), aqueous solution (A) and oily suspensions containing 0.5% w/v and 5% w/v aluminum stearate (1A and 1I, respectively).

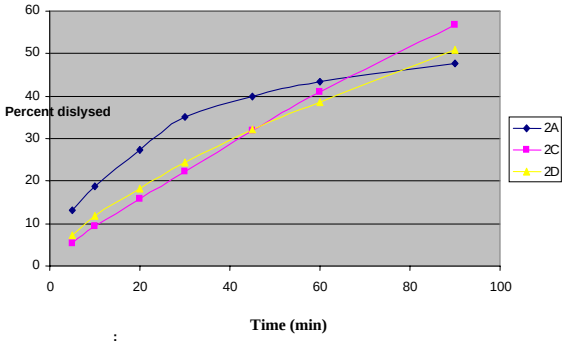

Figure 3: Plot of the percent of salicylate appearing in the dialysis medium versus time for an oily suspension (O), aqueous solution (A) and oily suspension containing 0.7% w/v lecithin in FCO (2A) and oily formulations (12) with or without 0.7% w/v lecithin (2C or 2D, respectively).

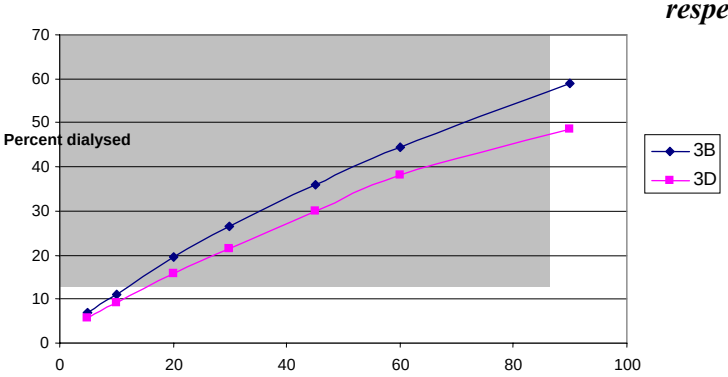

Figure 4: Plot of the percent of salicylate appearing in the dialysis medium versus time for an oily suspension (O), aqueous solution (A) and oily suspension containing 0.7% w/v lecithin in FCO (2A) and oily formulations (12) with or without 0.7% w/v lecithin (2C or 2D, respectively).

The time required for 30% and 50% of the salicylate to appear in solution outside the dialysis sac ($t_{30\%}$ and $t_{50\%}$) were calculated from the individual release rate curves for each formulation and were used as indices for estimating the release rate (Table 2). Table 2 also contains the viscosities of all formulations. [14]

Analysis of variance and Duncan`s test were carried out to distinguish the differences between the mean $t_{30\%}$ values. The results of the analysis can be summarized as shown in Table (3), where any two means that are not underlined by the same line are significantly different ($p< 0.05$ or $p < 0.01$) and any two means underlined by the same line are not significantly different.

The results given in Table (3) show that the sensitivity of the method in discriminating between the different formulations is not as good as might be expected from a simple comparison of the mean values of $t_{30\%}$. This reduction in sensitivity is brought about by the relatively low reproducibility of the release of salicylate from some of the systems. It is considered that this low reproducibility is related to the nature of the suspensions that are being tested and the complexity of the mechanisms that will influence the overall release process. These mechanisms are described in the discussion section.

A cumulative correction to account for the previously removed samples was not made when determining the percentage of drug released because, as can be seen from the following calculations which make use of data obtained for the simple suspension in the oil (O), the corrected and uncorrected values are approximately equal after 7 samples are removed. Equation 1, which was described by Bates et al. [15] was used to calculate the corrected values.

$$C_n = C_{n,meas.} + \frac{5}{1500} \sum_{s=1}^{n-1} (C_{s,meas.}) \qquad (\text{Eq. 1})$$

Where $C_{n,\,meas.}$ denotes the spectrophotometrically measured concentration (expressed as % in this case), C_n is the concentration (% in this case) of the n^{th} sampling expected in the dialysis medium if the previous samples had not been removed and $\sum_{s=1}^{n-1}(C_{s,meas.})$ is the sum of concentrations (% in this case) measured spectrophotometrically from sample 1 to (n-1) sample. A corrected value (C_n) of 49.2% is obtained when Eq.1 is applied to the data provided by formulation (O) after 7 samples have been removed. As can be seen from Table (1) the uncorrected value ($C_{n,meas.}$) is 48.6%, which is only 0.6% less than the corrected value and in the case of the aqueous solution (A) the difference is only 0.95%. In the case of the 1^{st}, 2^{nd}, 3^{rd}, 4^{th}, 5^{th}, and 6^{th} samples the differences between corrected and uncorrected values will be less than 0.6% and 0.95% in the oily and aqueous systems, respectively.

Table 2: Apparent viscosities, $t_{30\%}$ and $t_{50\%}$ values for sodium salicylate formulations.

Type of vehicle (a)	*$t_{30\%}$ (min) (b)*	*η_{app} (mN s m^{-2}) (C)*	*$t_{50\%}$ (min) (b)*
O	*22.2±5.1*	*17.5*	*> 90*
A	*14.3±4.7*	*0.695*	*28.6*
1A	*34.0±6.1*	*37*	*> 90*
1B	*37.1±5.2*	*50*	*> 90*
1C	*45.3±5.9*	*59*	*> 90*
1D	*50.7±5.8*	*69*	*> 90*
1E	*51.5±6.3*	*81*	*> 90*
1F	*58.3±6.1*	*92*	*> 90*
1G	*89.2±6.8*	*104*	*> 90*
1H	*99.7±6.4*	*144*	*> 90*
1I	*110.0±6.2*	*176*	*> 90*
2A	*22.7±4.6*	*23*	*> 90*
2B	*22.9±4.9*	*40*	*> 90*
2C	*42.2±5.8*	*120*	*76.5*
2D	*41.1±5.6*	*105*	*87.5*
3A	*36.7±5.6*	*51*	*75.0*
3B	*35.3±5.9*	*83*	*71.0*
3C	*38.6±5.8*	*98*	*76.5*
3D	*44.4±6.3*	*131*	*> 90*

A. See Table 2 for formulation code.
B. Each value is the mean of 3 experiments ± SD.
C. η_{app}, apparent viscosity. [14]

Table 3: Summary of the results of the statistical analysis of $t_{30\%}$ values for formulations containing sodium salicylate.

Formulation[(a)]	A	O	2A	2B	1A	3B	3A	1B	3C	2D	2C	3D	1C	1D	1E	1F	1G	1H	1I
Mean value of $t_{30\%}$ in rank order (b)	14.3	22.2	22.7	22.9	34.0	35.3	36.7	37.1	38.6	41.1	42.2	44.4	45.3	50.7	51.5	58.3	89.2	99.7	110
p = 0.01																			
P = 0.05	A	O	2A	2B	1A	3B	3A	1B	3C	2D	2C	3D	1C	1D	1E	1F	1G	1H	1I

A. ***See Table 2 for formulation code.***
B. ***Any two means not underlined by the same line are significantly different (p< 0.05 or p < 0.01) and any two means underlined by the same line are not significantly different.***

Discussion

The simplest test formulation that was used in this method was the aqueous solution of sodium salicylate (formulation A). However, even in this system the overall release rate of the drug cannot be ascribed solely to the rate of dialysis of a single species in solution, because other reactions will be occurring as indicated by the simplified scheme in Figure (5).

Thus, the observed rate of release will be influenced not only by the dialysis rates of salicylate ion and undissociated salicylic acid, but also by the rate of dissolution of any particles of precipitated salicylic acid. If this precipitation produces fine particles, then subsequent dissolution will be fairly rapid and the release rate will not be decreased markedly. [7] In fact, this aqueous solution provided the most rapid release rate of all the systems that were studied and gave mean $t_{30\%}$ and $t_{50\%}$ values of 14.3 and 28.6 min, respectively (Tables 2 and 3).

The mechanism of releasing drug from the oily suspensions of sodium salicylate is likely to be more complex than from the aqueous solution. This is because (a) partition of salicylate between oily and aqueous phases must occur, (b) the oil can act as a reservoir for salicylic acid, formed by hydrolysis of the sodium salt and (c) some of the acidic aqueous dissolution medium penetrates through the dialysis membrane into the sac, particularly when sucrose is used as an ingredient in the oily vehicle. In addition, the release of water-soluble compounds, such as sucrose into the aqueous dissolution medium, the sedimentation of sodium salicylate to the bottom of the oily vehicle inside the dialysis sac and the possibility of emulsification inside the dialysis sac may affect the release of salicylate.

In spite of the additional processes involved when oil is used as the suspension vehicle (formulation O), the initial rate of release of salicylate, as indicated by the $t_{30\%}$ value, is not much slower than from the aqueous solution (A). The mean $t_{30\%}$ values are 22.2 min for (O) and 14.3 min for (A), but the statistical analysis of the results (Table 3) indicated that this difference was insignificant at $p > 0.05$. It is possible that precipitation of salicylic acid from the aqueous solution (A) may be partly responsible for this similarity in the initial rates of release. However, the release rate from the oily suspension decreased at longer times in comparison with the aqueous solution and the $t_{50\%}$ values were > 90 min for (O) and only 28.6 min for (A) (Table 2). This difference may arise from the effect of the oil (formulation O) acting as a reservoir for salicylic acid; and so interfering in the apparent

rate of appearance of salicylate in the aqueous dissolution medium. This difference indicates that the dialysis rate is not the rate limiting step in the release process, and the method appears, therefore, to satisfy the conditions given by Swarbrick [16] and Shah and Sheth [8] for the determination of drug release from dosage forms using dialysis techniques.

Table (2) shows that, with few exceptions, a rank order correlation exists within each type of formulation (i.e. Types 1, 2, or 3) between $t_{30\%}$ and the apparent viscosity of the different vehicles.

In fact, the correlation coefficient (r) for the values given by all the formulations is 0.8127 ($p < 0.001$). This rank order suggests that although the gels are affected by the presence of water, as indicated by the preliminary studies, the viscosity of the systems still retards the release of drug, at least in the early stages. This finding is in agreement with that reported by previous studies [17] who found that increasing the concentration of aluminium stearate in the oil delayed the absorption of penicillin from an i.m. depot injection. They suggested that this is because of the entrapment of the drug particles within the gels.

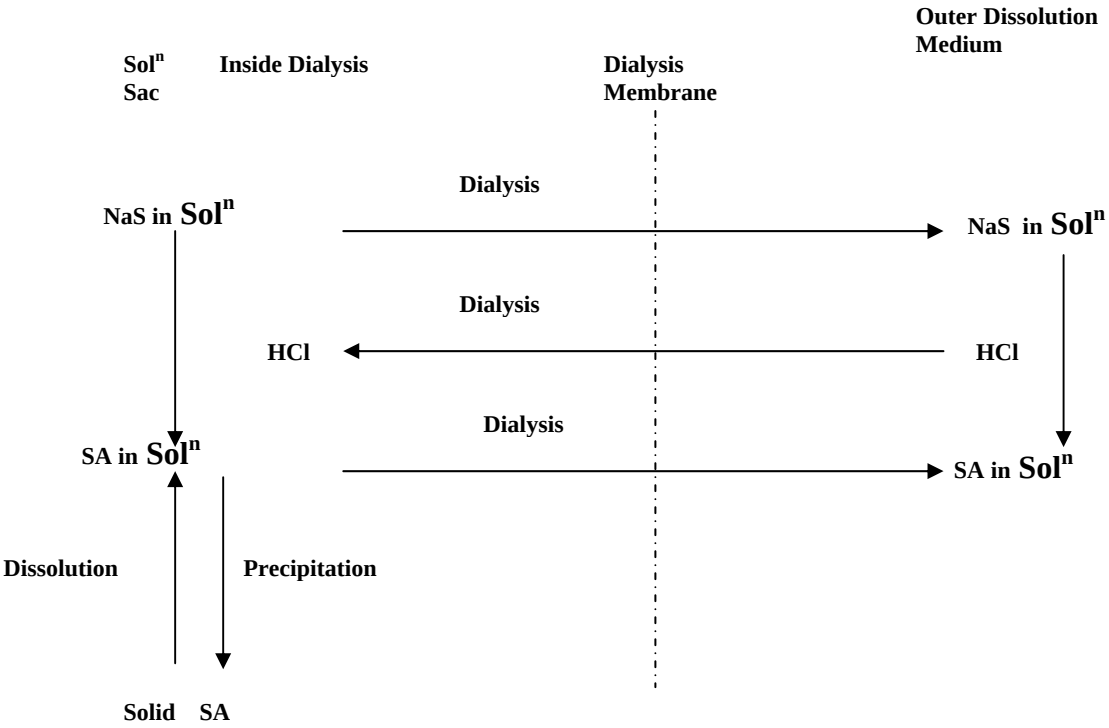

Fig. (5): Reactions occurring during dialysis of sodium salicylate solution into an acidic dissolution medium (Nas = Sodium salicylate and SA = salicylic acid).
Note: The effects of dissociation of the salicylic acid and its sodium salts are ignored in this scheme.

In the case of sucrose-containing formulations (2C, D and 3 A, B, C and D), osmotic imbalance between inside and outside the dialysis sac caused the influx of appreciable volumes of the aqueous phase. In the earlier stages, these formulations exhibited slow release rates compared to formulation (O) and some other oily vehicles, (Table 2), probably because of their high viscosities. However, with the exception of formulation 3D, behaviour of whose might be due to its very high viscosity and the adsorptive capacity of its Cab-o-sil content, these sucrose-containing formulations were the only oily suspensions that gave $t_{50\%}$ values of < 90 min. (Table 2). These increases in release rates in the later stages were accompanied by the influx of aqueous phase, the volume of which was about the same as that of the oily liquid, i.e. 5 ml, after 90 min. In the presence of water, these oily vehicles form relatively large pear-shaped globules, inside which the sucrose and other solid ingredients sedimented leaving a clear oily layer at the top of the globules. The size of these globules ranged from approximately 1-10 mm and their overall densities caused them to fall to the bottom of the dissolution flask. As the sucrose was removed from the globules by dissolution into the aqueous phase, they gradually disappeared and the oil then formed a layer on the surface of the aqueous phase. The lifetime of these globules appeared to depend on the dissolution rate of sucrose, which, in turn, will depend on the viscosity of the oily liquid inside the globules. Thus, the lifetime of the globules formed by formulation 3A (20% sucrose in FCO) was only of the order of 5 minutes so that an oily layer was formed on the surface of the dissolution medium in a relatively short time. The viscosity of this layer was presumably similar to that of FCO alone; and the release of salicylate from 3A would therefore be expected to be not too much slower than from a suspension in FCO (O) (Tables 2 and 3).

The lifetime of the globules produced by the remaining sucrose-containing formulations fell into the order 3B < 3C < 3D. These formulations also contain Cab-o-sil in 0.3%, 0.5% and 1% concentrations, respectively, and the rank order is in accordance with their viscosities (Table 2).

Thus, the higher viscosities will delay the loss of sucrose from the globules and the release of salicylate not only from the globules but also from the oily layer that is eventually produced on the surface of the dissolution medium; particularly with the formulation 3D, which is the most viscous oily formulation. Thus, the influx of water will not only affect the viscosity of the oily vehicle but will also enhance the rate of partition of drug between oil and water because of the increase in interfacial area between these two phases.

The present results suggest that the release of salicylate from a suspension of its sodium salt in FCO can be influenced by the inclusion of:

A. Aluminium stearate, which retards the release, particularly when its concentration is 1.5% w/v or more,
B. Sucrose, which tends to give rise to a faster release in the later stages, and
C. Cab-o-sil, which tends to nullify the effects of sucrose, when used in a concentration of 1% w/v.

Furthermore, the inclusion of 0.7% w/v lecithin or 0.35% w/v hydrogenated castor oil in the oily vehicle does not appear to have any significant effects on the release process as shown by a comparison of the results obtained for formulations 2A and 2B, respectively, with that for the simple oily suspension (O). In fact, these three oily formulations were the only ones that gave $t_{30\%}$ values that were not significantly different to that given by the aqueous solution of sodium salicylate (A). The $t_{50\%}$ values were, of course, all much greater than that of (A). The insignificant effect of 0.7% w/v lecithin is also indicated by a comparison to the $t_{30\%}$ values obtained for formulations 2C and 2D.

Finally, there appears to be little difference in the *in vitro* release of salicylate from formulations that correspond to those patented by Stephens and Su [12] and Lin and Pramoda, [13] as shown by

a comparison of systems 2C and 3C, provided that the concentration of Cab-o-sil in Lin and Pramoda`s formula does not exceed 0.5% w/v, because if 1% is used, the increased rate of release, produced by sucrose in the later stages of release, is not so readily apparent.

Conclusion

It is suggested that oily vehicles that contain aluminium steate, lecithin, hydrogenated castor oil, sucrose and Cab-o-sil can be used as a depot preparations for chronic disease conditions. The enhancing effect of sucrose on the release rate of salicylate can be beneficial if acute *in vivo* response is required. Extrapolation of this study on tablets, capsules and i.m injection formulations is suggested and is being under progress in our laboratory.

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دراسة تأثير المواد الصيدلانية المختلفة في تحرير ساليسلات الصوديوم من المحاليل الزيتية

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الملخص

الهدف: هدف البحث هو دراسة تأثير المواد الصيدلانية المختلفة في تحرير ساليسلات الصوديوم من المحاليل الزيتية.

الأدوات: تم تحضير عدة صيغ لزيت جوز الهند المجزأ (FCO) محتوية على مختلف المواد الصيدلانية. تمت دراسة معدل تحرير الساليسلات من هذه الصيغ الزيتية باستعمال طريقة الديلزة. تم اعتماد الوقت اللازم لظهور 30% و 50% من الساليسلات في المحلول خارج كيس الديلزة كمؤشر لتقييم معدل التحرير.

النتائج: دلت نتائج البحث على ان ستياريت الألمنيوم تعيق معدل تحرير الساليسلات وخاصة بتركيز 1.5% فأكثر. الصيغة الزيتية المحتوية على 0.5% ستياريت الألمنيوم + 0.7% لسثين+ 0.35% زيت الخروع + 20% سكروز في الـ FCO وكذلك الصيغة الزيتية المحتوية على 0.5% كا ب – أو – سيل + 20% سكروز في FCO تؤخر معدل تحرير الدواء.

إن ادراج السكروز، على اي حال، في الصيغ المدروسة يعقد الحالة ويحسن تحرير الدواء وخاصة في المراحل الأخيرة. أما ادراج 1% كاب– أو – سيل فقد ابطل التأثير الحسن للسكروز في معدل التحرير. وقد نوقشت الأسباب الممكنة لهذه التأثيرات مع الإشارة والتركيز الى ميل السكروز لتكوين الكريا ت بسبب التأثير التنافذي داخل كيس الديلزة.

الخاتمة: يمكن اعتماد الصيغ الزيتية، مثلا : (0.5% ستياريت الألمنيوم + 0.7% لسثين + 0.35% زيت الخروع + 20% سكروز في FCO) و(0.5% كاب –أو – سيل + 20% سكروز في FCO) كمستودعات طويلة الأمد في حالات الأمراض المزمنة. و يمكن الاستفادة من السكروز في تحسين معدل تحرير الساليسلات في حالات الأمراض الحادة. ويقترح امتداد هذه الدراسة لتشمل الحبوب والكبسولات ومحاليل الزرق العضلي.

الكلمات الدالة: معدل تحرير ساليسلات الصوديوم، المركبات الزيتية، المواد الصيدلانية المضافة، زيت جوز الهند المجزأ.