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Research Article

Glucono-Delta-Lactone Mitigates the Erythrocyte Sedimentation Rate of Human Blood

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Abstract:
The clumping of circulating blood cells in many diseases gives rise to serious complications. The sed-rate has been used to monitor blood for these changes. The protective low molecular weight agent used in this study was found to suppress the elevated sed-rate values.

Keywords: Glucono-delta-lactone, erythrocyte sedimentation rate, cell agglutination

I. Introduction

Definitions:

The erythrocyte sedimentation rate (ESR), defined as the distance erythrocytes settle out of an anticoagulated sample of human whole blood in one hour, serves as an indirect measurement of the rate of erythrocyte agglutination. It is useful as a non-specific biomarker of inflammation, and it has been shown to be significantly elevated by infectious disease states [1], and by metabolic syndrome [2]. Methylcellulose (MC) is a polymer that is known to significantly accelerate the ESR. Glucono-delta-lactone (GDL) is a naturally occurring oxidation product of glucose used widely in food processing and cosmetics as a curing and thickening agent.

Objective:

Surface-to-surface adhesion of adjacent erythrocytes in human blood, produced by the interaction of compounds bound to or associated with their cellular membranes, leads to masses of agglutinated red blood cells which can impede blood flow through the microcirculation of the body. This reaction is instigated by inflammatory and necrotic processes, and serves to worsen these pathological states by causing obstructive hypoxia. The purpose of this experiment is to examine the usefulness of GDL as a mediator of erythrocyte agglutination. If GDL can be shown to mitigate the agglutinative effects of MC, then it may show promise as a treatment for the thickening of blood associated with many pathologies.

Experimental Design:

The experiment will be conducted in two parts. Fixed concentrations of MC and GDL in whole blood, both separately and in conjunction, will be examined for their effects on the ESR. A titration of MC-treated blood with varying concentrations of GDL will then be prepared and the ESR of each dosage will be taken to determine a dose-response relationship. Measurement of the ESR will be taken every 30 minutes to observe the temporal dynamic of the sedimentation.

II. Materials and Methods

Expired citrated whole bloods (CWB) were obtained from the University Hospital's clinical laboratories. The bloods were then pooled into samples (n=17) of approximately 5 mL each. Nine samples were used in the first portion of the experiment. Each sample was divided into four aliquots of 1 mL each: a distilled water dilution, a solution of MC, a solution of GDL, and a solution containing both MC and GDL. (*Table 1*)

Table 1: Aliquots prepared for examination of MC and GDL effects on the ESR

Aliquot	Reagent(S)	Sample (Cwb)	Final Concentration
Control	120 µL distilled H_2O	880 µL	(water dilution)
MC	100 µL 1% MC (aq)	900 µL	0.1% MC
GDL	100 µL 40 mg/mL GDL (aq)	900 µL	4 mg/mL GDL
MC + GDL	100 µL 1% MC (aq) + 40 µL 100 mg/mL GDL (aq)	860 µL	0.1% MC / 4 mg/mL GDL

Eight samples were used in the second portion of the experiment. Each sample was divided into four aliquots of 1 mL each: a control solution of MC and three GDL titrations of that control (1 mg/mL, 2 mg/mL and 3 mg/mL). (*Table 2*)

Table 2: Aliquots prepared for examining effects of GDL titration on the ESR of MC-treated blood

Aliquot	Reagent(S)	Sample (Cwb)	Final Concentration
Control	100 µL 1% MC (aq) +20 µL distilled H_2O	880 µL	0.1% MC
1 mg/mL GDL	100 µL 1% MC (aq) +10 µL 100 mg/mL GDL (aq)	890 µL	0.1% MC +1mg/mL GDL
2mg/mL GDL	100 µL 1% MC (aq) +20 µL 100 mg/mL GDL (aq)	880 µL	0.1% MC +2mg/mL GDL

3 mg/mL GDL	100 µL 1% MC (aq) +30 µL 100 mg/mL GDL (aq)	870 µL	0.1% MC +3 mg/mL GDL

All aliquots were prepared in 5 mL 12x75 mm polystyrene round-bottom test tubes. Following mixing, aliquots were incubated at 37° C for 20 minutes.

An ESR was then performed on each bank of samples. Blood, in the amount of 0.5 mL, was suctioned from each aliquot into 1 mL graduated glass pipettes. These pipettes were then sealed at the tip and stood vertically. A measurement of erythrocyte sedimentation, in the form of the length of the plasma column above the settled erythrocytes in each pipette, was taken every 30 minutes. Samples were timed individually, so as to ensure that the time value for each measurement was as accurate as possible.

Paired *t* tests and analyses of variance (with a value of $p < 0.05$ assumed to indicate significance) were performed using GraphPad's InStat statistical program.

III. Results

The first portion of the experiment examined the effects of MC and GDL, individually and together, on the ESR. The results are presented in *Table 3*. Relative to the control at each interval, MC significantly increased the ESR (two-tailed $p < 0.004$) and GDL significantly decreased the ESR (two-tailed $p < 0.002$). The addition of GDL significantly mitigated the effects of MC (two-tailed $p < 0.005$) at all times.

Table 3: Effects of MC and GDL on the ESR (mm ± SD)

	30 MIN.	**60 MIN.**	**90 MIN.**
Control	19.8 ± 12.3	28.8 ± 13.3	34.2 ± 11.0
MC	39.6 ± 9.3	43.7 ± 7.1	45.2 ± 6.1
GDL	9.6 ± 7.2	20.9 ± 11.2	27.2 ± 11.8
MC + GDL	30.1 ± 9.0	38.6 ± 6.2	40.7 ± 6.1

The second portion of the experiment examined the dose-response of blood containing 0.1% MC to a titration of GDL. The results are presented in *Table 4*. Relative to the control at each interval, all concentrations of GDL significantly reduced the ESR (one-tailed $p < 0.05$). However, the concentrations of GDL did not produce significantly different effects in comparison with one another (one-tailed $p > 0.07$).

Table 4:ESR values for GDL titration of MC-treated blood (mm ± SD)

	30 MIN.	**60 MIN.**	**90 MIN.**
Control	40.5 ± 6.6	43.9 ± 5.7	45.0 ± 5.4
1 mg/mL GDL	34.6 ± 10.8	39.3 ± 8.8	40.9 ± 7.8
2 mg/mL GDL	35.5 ± 12.0	40.0 ± 9.5	42.0 ± 8.2
3 mg/mL GDL	33.5 ± 11.4	39.6 ± 8.0	42.0 ± 6.8

IV. Discussion

The results of this experiment indicate that GDL is an effective mediator of the ESR. GDL alone was shown to significantly reduce the ESR relative to the control, and in all cases significantly mitigated the agglutinative effects of MC The results of this experiment indicate that GDL is an. The results of the experiment regarding the titration of MC with GDL are inconclusive. Although GDL significantly reduced the ESR relative to the MC control at every dosage, the results do not differ significantly from one another. A clear dose-response pattern cannot be established with these data. It is worth noting, however, that the essentially flat response across all dosages would seem to indicate that whatever mechanism GDL operates by in whole blood is saturated at a concentration of 1 mg/mL. If so, much smaller amounts of GDL could potentially be effective.

The results of this experiment warrant further testing of GDL as a mediator of hematological homeostasis.

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