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Anti-inflammatory activity of new complexes of SnCl4 with salicyloyl hydrazones of benzaldehyde and 4-bromobenzaldehyde on different models of inflammation.

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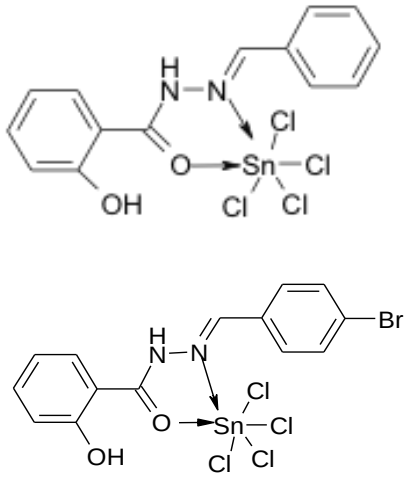
Anti-inflammatory activity of new complexes of SnCl4 with salicyloyl hydrazones of benzaldehyde and 4-bromobenzaldehyde on different models of inflammation.



Abstract: This research is devoted to the study of the anti-inflammatory properties of complexes of $SnCl_4$ with salicyloyl hydrazones of benzaldehyde and 4-bromobenzaldehyde, as well as salicylic acid, benzaldehyde and 4-bromobenzaldehyde on the model of inflammation caused by the injection of histamine, trypsin, carrageenan and formalin. The paper presents new data on the anti-inflammatory activity of the studied complexes in the range of 1 - 24 hours and 1-16 days after the start of the experiment.

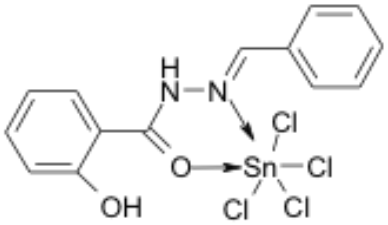
Keywords: salicyloyl hydrazones; benzaldehyde; inflammation; complex compounds

Introduction

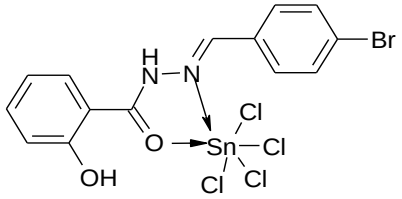
Currently, one of the most important and studied problems in medicine is inflammation. It is considered that inflammation is a protective-adaptive response of the body to the pathogenic stimulus and to the damage caused by it, which was formed during the evolution process. Inflammation refers to the fundamental pathological processes that constitute the pathophysiological basis of most human diseases. Modern medicine knows a large number of anti-inflammatory drugs, both from the groups of steroid and non-steroid drugs.

With the simultaneous intake of components of combined preparations into the body, a number of advantages can be observed: the therapeutic effect of the components of the complex is enhanced, these drugs are more easily tolerated by patients and prevent the occurrence of polypragmasy during therapy. For us it was of interest to study the anti-inflammatory properties of complexes of $SnCl_4$ with salicyloyl hydrazones of benzaldehyde and 4-bromobenzaldehyde, as well as compounds that contain functional groups that are part of the complexes.

To study the possible mechanisms of action of complex compounds, as well as the contribution of functional groups included in the complexes, the following models of inflammation were used: trypsin, histamine, carrageenan and formalin induced.



Complex I



Complex II

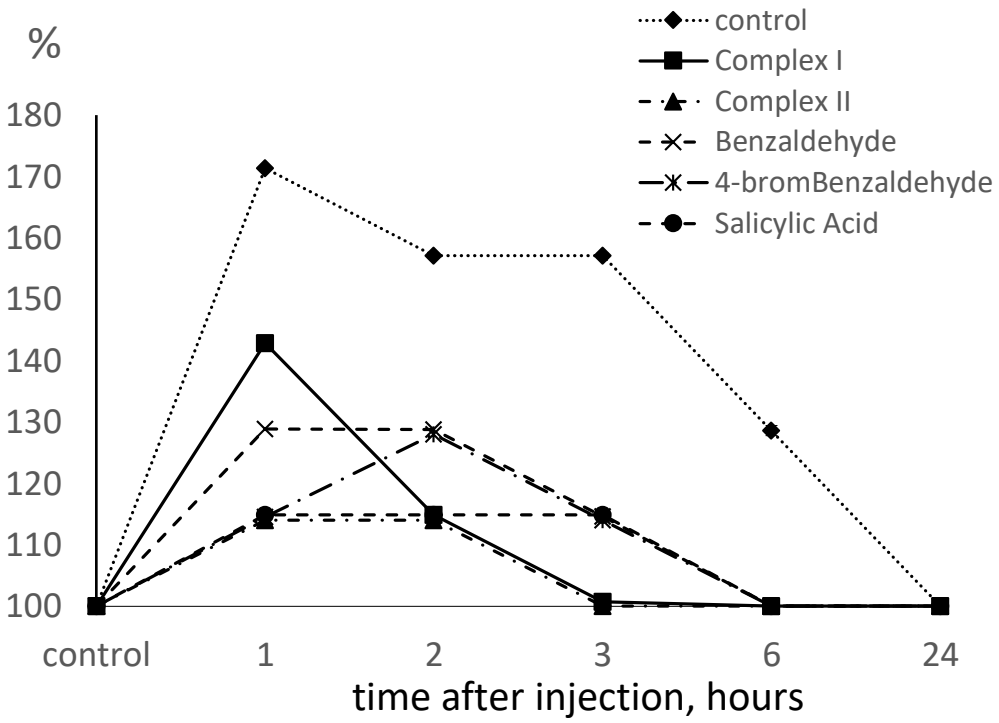
Studies were conducted on 24 groups of animals, 5 pcs each, for every type of inflammation model. During the modelling trypsin and histamine inflammation, the test substances were administered 30 minutes before the injection of the inflammatory agent. Treatment by oral administration of certain components began a day after the development of inflammation on the carrageenan inflammation model and three days later on the formalin model.

Each experimental group of animals received orally: 1-4 group – control group, 5-12 groups - were administered emulsion solutions of SnCl4 complexes with salicyloyl hydrazone of benzaldehyde (I) and salicyloyl hydrazine of 4-bromobenzaldehyde (II) in terms of the remainder salicylic acid (40 mg/kg), respectively; 13-17 – emulsion of benzaldehyde in tween; 18 – 20 – emulsion of 4-bromobenzaldehyde in tween; 21- 24 – groups were treated by salicylic acid solution.

Results and discussion

Trypsin inflammation (volume)

Animals which were administered complex compounds I and II, three hours after the start of the experiment, the size and color of the injured paw returned to its native state. Salicylic acid has an anti-inflammatory effect similar to complex compound II, six hours after administration of salicylic acid, the volume of the affected paw reached the control values.



The volume of the affected paw after the introduction of benzaldehyde and 4-bromobenzaldehyde reached the control after 6 hours after the start of the experiment.

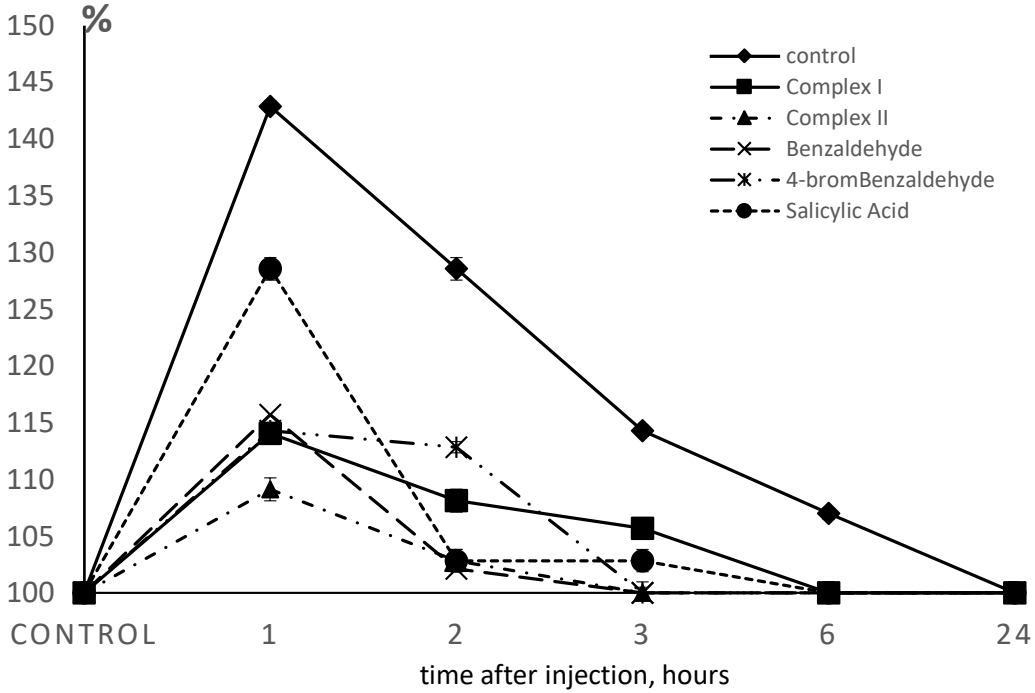
Trypsin inflammation (width)

The dynamics of changes in the width of the injured paw with its profile is similar to the change in volume. Control indicators were achieved only in 24 hours after the injection by trypsin, which is apparently related with the physiology of resorption.

Compound / Time, hours	Control group	Complex I	Complex II	Benzaldehyde	4-brombenzaldehyde	Salicylic acid
Control	100 ± 0,1	100 ± 0,1	100 ± 0,1	100 ± 0,1	100 ± 0,1	100 ± 0,1
1	171,7 ± 0,1	154,3 ± 0,1	147,8 ± 0,2	131,3 ± 0,2	139,1 ± 0,4	145,7 ± 0,3
2	169,6 ± 0,2	147,8 ± 0,2	143,5 ± 0,1	125,0 ± 0,2	132,6 ± 0,2	139,1 ± 0,3
3	152,2 ± 0,1	139,1 ± 0,1	139,1 ± 0,1	121,7 ± 0,1	123,9 ± 0,5	130,4 ± 0,3
6	143,5 ± 0,2	123,9 ± 0,1	121,7 ± 0,1	117,4 ± 0,1	119,6 ± 0,6	121,7 ± 0,2
24	100 ± 0,1	100 ± 0,2	100 ± 0,1	100 ± 0,1	100 ± 0,2	100 ± 0,2

Histamine inflammation (volume)

The data depicted show that complex compounds I and II have a visible anti-inflammatory effect on the histamine inflammation model. There are no significant statistical differences between the anti-inflammatory activity of complex I and complex II; for example, 6 hours after the start of the experiment, the volume of the affected limb reached the control.



Salicylic acid also exerts a marked anti-inflammatory effect, but somewhat inferior efficiency than complex compounds. On the histamine inflammation model, benzaldehyde and 4-bromobenzaldehyde also have pronounced anti-inflammatory activity.

Thus, one hour after the start of the experiment the volume of the affected paw with benzaldehyde increased by 15%, and after three hours the volume of the affected limb with benzaldehyde and 4-bromobenzaldehyde reached the reference value.

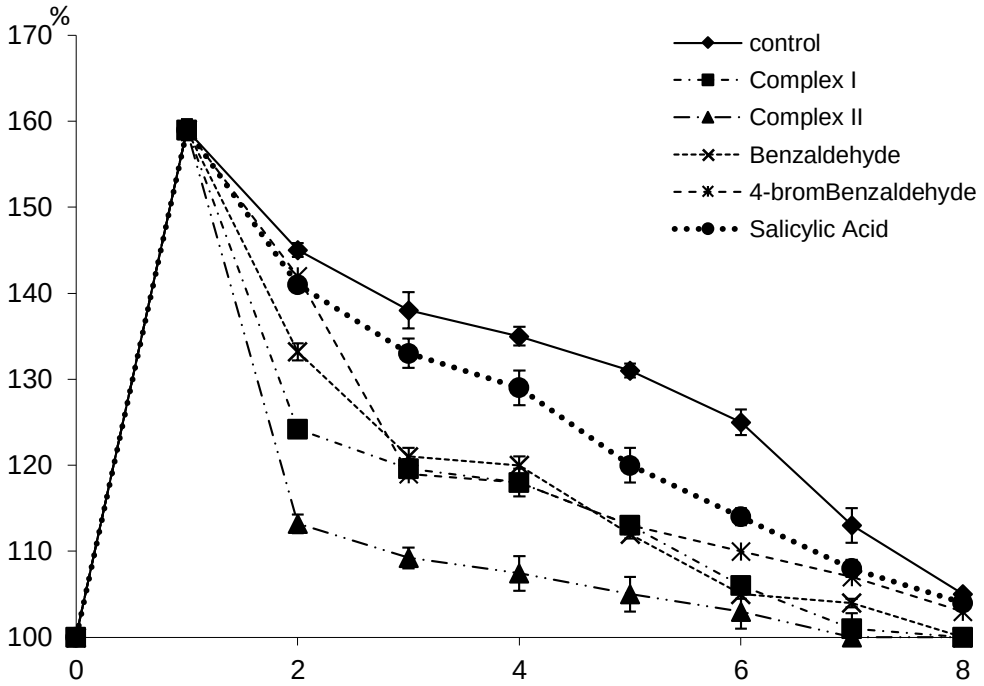
Histamine inflammation (width)

Compound / Time, days	Control group	Complex I	Complex II	Benzaldehyde	4-brombenzaldehyde	Salicylic acid
control	100 ± 2,1	100 ± 2,1	100 ± 2,1	100 ± 2,1	100 ± 2,1	100 ± 2,1
1	151,2 ± 2,1	112,7 ± 1,1	117,6 ± 2,2	139,5 ± 1,8	130,2 ± 2,2	122,7 ± 2,0
2	130,2 ± 3,0	104,7 ± 1,1	108,1 ± 2,2	125,6 ± 1,8	127,9 ± 1,0	109,3 ± 2,3
3	118,6 ± 2,0	100 ± 1,1	100 ± 2,3	114 ± 1,8	116,3 ± 2,0	104,7 ± 2,3
6	114 ± 2,0	100 ± 2,0	100 ± 2,3	109,3 ± 1,8	111,6 ± 2,3	100 ± 2,0
24	100 ± 2,0	100 ± 2,3	100 ± 2,3	100 ± 1,8	100 ± 2,0	100 ± 2,3

The study of the dynamics of changes in the width of the affected paw, after the injection of complex compounds I and II and the compounds that are included in their structure, showed that this indicator coincides with the indicators of changes in the volume of the injured paw.

Carrageenan inflammation (volume)

From the obtained data, it is clear that salicylic acid, as well as benzaldehyde and 4-bromobenzaldehyde, have an anti-inflammatory effect, which leads to a decrease in the inflammatory process during the first days of the experiment. Six days after the start of the experiment, the volume of the affected paw for animals that were administered complex compounds I and II, benzaldehyde and salicylic acid almost reached the control values.

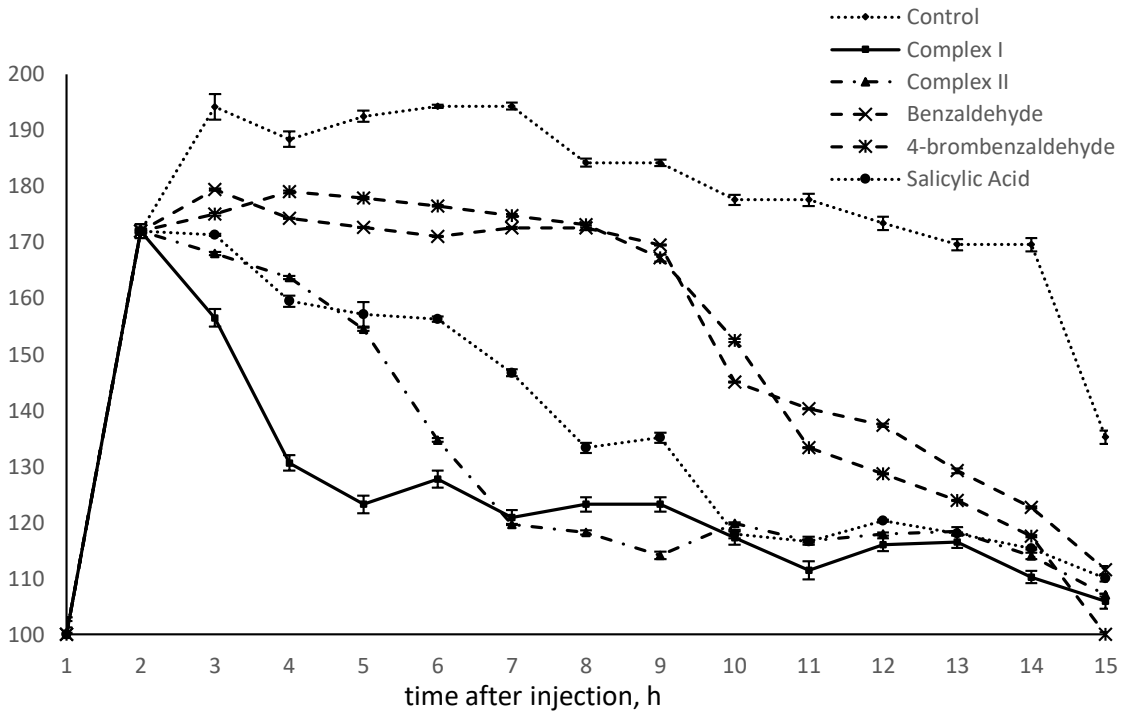


Carrageenan inflammation
(width)

Compound / Time, days	Control group	Complex I	Complex II	Benzaldehyde	4-brombenzaldehyde	Salicylic acid
0 (control)	100 ± 2,4	100 ± 2,3	100 ± 2,4	100 ± 3,0	100 ± 3,0	100 ± 2,4
1	157 ± 3,4	157,3 ± 3,4	157 ± 3,4	135 ± 7,0	135 ± 7,0	157 ± 3,4
2	158 ± 3,9	128 ± 2,6	109 ± 4,6	132 ± 2,0	134 ± 8,0	142 ± 4,5
3	148 ± 8,3	125,6 ± 7,3	109 ± 4,9	125 ± 3,0	128 ± 9,0	128 ± 4,4
4	151 ± 4,7	124,4 ± 5	107 ± 4,2	123 ± 4,0	137 ± 8,0	125 ± 4,7
5	143 ± 4,0	119,3 ± 5,0	113 ± 5,0	116 ± 3,0	123 ± 5,0	117 ± 5,3
6	139 ± 3,8	111,7 ± 3,3	111 ± 4,0	112 ± 2,0	115 ± 3,0	110 ± 2,8
7	126 ± 6,8	102,7 ± 1,8	109 ± 5,0	106 ± 3,0	109 ± 4,0	105 ± 1,3
8	122 ± 5,4	100,2 ± 3,1	101 ± 2,0	101 ± 2,0	102 ± 2,0	107 ± 6,8
9	115 ± 2,0	100,1 ± 2,0	100 ± 1,0	100 ± 1,8	100 ± 1,1	104 ± 2,5

It should be noted that the change in the dynamics of the width of the inflamed paw is similar to the changes in the volume of the affected paw and does not show statistical differences.

Formalin inflammation (volume)



Starting from the second day of treatment with complex I, the volume of the affected paws of rats decreased by 19%, and this trend continued the following days of the experiment.

Benzaldehyde and 4-bromobenzaldehyde also exhibited anti-inflammatory activity; on the 14th day of treatment, the volume of the affected paws reached baseline.

Better anti-inflammatory activity was shown for salicylic acid. The volume of rats paws decreased by 37% on the 7th day of the treatment. But in this experiment the volume of the affected paws did not return to the initial level until the end of the experiment

Formalin inflammation (width)

Compound Time, days	Control group	Complex I	Complex II	Benzaldehyde	4-brombenzaldehyde	Salicylic acid
0 (control)	100 ± 0,2	100 ± 0,2	100 ± 0,2	100 ± 0,2	100 ± 0,2	100 ± 0,2
3	150,5 ± 0,2	150,5 ± 0,2	150,5 ± 0,2	150,5 ± 0,1	150,5 ± 0,1	150,5 ± 0,2
4	165,1 ± 0,2	135 ± 0,2	151,8 ± 0,2	158,2 ± 0,4	154,8 ± 0,1	153,4 ± 0,2
5	162,3 ± 0,2	132,7 ± 0,1	143,4 ± 0,2	145,9 ± 0,4	152 ± 0,1	150,3 ± 0,1
6	160,3 ± 0,2	136 ± 0,2	141,7 ± 0,1	135 ± 0,6	140,3 ± 0,1	148,3 ± 0,2
7	159,7 ± 0,2	135,3 ± 0,2	134,7 ± 0,1	132 ± 0,1	137 ± 0,1	145,4 ± 0,2
8	158 ± 0,1	131,6 ± 0,2	134,8 ± 0,1	135 ± 0,1	137 ± 0,1	143,4 ± 0,2
9	162 ± 0,2	135,6 ± 0,1	138,7 ± 0,1	135 ± 0,1	135 ± 0,1	140,8 ± 0,2
10	160,3 ± 0,2	132,7 ± 0,2	135,1 ± 0,2	128 ± 0,1	129 ± 0,2	139,3 ± 0,1
11	149,9 ± 0,2	122 ± 0,2	122,9 ± 0,2	123 ± 0,1	128,3 ± 0,2	130,3 ± 0,1
12	147,9 ± 0,1	121,5 ± 0,1	120,5 ± 0,1	121 ± 0,1	125 ± 0,2	125 ± 0,2
13	145,0 ± 0,2	111,1 ± 0,2	114,4 ± 0,1	117 ± 0,2	118 ± 0,1	117,1 ± 0,2
14	138 ± 0,1	111,5 ± 0,1	115,7 ± 0,2	115 ± 0,1	115 ± 0,1	109,5 ± 0,2
15	127 ± 0,1	109 ± 0,1	107 ± 0,2	110 ± 0,1	115 ± 0,1	109 ± 0,2
16	124 ± 0,1	106 ± 0,2	104 ± 0,2	105 ± 0,1	106 ± 0,2	109 ± 0,2

Conclusions

Thus, in the course of the experiment, it was found that complex compounds I and II exhibited the best anti-inflammatory activity in all models of inflammation. Certainly, the components of complex compounds I and II, salicylic acid and benzaldehydes make their contribution into the anti-inflammatory activity of the complexes.