STUDIES ON ADSORPTION CHLORAMFENICOL ON CHITOSANS IN PHARMACEUTICAL "*IN VITRO*" MODEL

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Abstract
In clinical practice in the treatment of obesity, uses several natural macromolecular compounds, whose functioning is based on supporting the weight loss. In use of dietary supplements containing chitosan, sometimes reaches the illness and in the treatment, which the other therapeutic agents are chemotherapeutic drugs. The aim of our study was to determine the binding capacity of chloramphenicol chemotherapeutic depending on variable factors physico-chemical properties, present in the intestinal tract model of chitosans present in the drugs. The phenomenon of adsorption of chloramphenicol was examined by a dynamic model simulating the conditions of the pharmaceutical in vitro, the amount of adsorbed chemotherapy. The obtained results show that chloramphenicol is adsorbed by chitosans at pH ranges used, and the binding capacity depends on the pH of the environment and the viscosity and concentration of the chemotherapeutic agent as well as the type of chitosan and the additional substances present in the gastrointestinal tract. The average size of the adsorption system chemotherapeutic chitosan-nutrients depending on the pH of the medium ranged from 22.3 to 100.0%. Maximum number of adsorption points above pH 7 (chitosan precipitated polymer forming the emulsion-gel system).

Key words: *Chloramphenicol, chitosan, absorption.*

1. Introduction

In the treatment of obesity, the use of natural compounds were present, whose functioning is based on supporting weight loss by being able to absorb dietary factors. These compounds form a polymeric gel in contact with water, have the ability to adsorb nutrients and other components that will be in the vicinity..

Application for healing various antibacterial active substance together with nutritional supplements containing chitosan may lead to changes in bioavailability of the drugs tested. Chloramfenicol (chloromycetin, Detreomycin) 2,2-dichloro-N-[(1R,2R)-1,3-dihydroxy-1-(4-nitrophenyl)propan-2-yl] acetamide is an antibiotic with bactericidal action and bacteriostatic used also in the treatment of rickettsiae, mycoplasma and chlamydia. The mechanism of action is the inhibition of protein synthesis by binding to the 50S ribosomal subunit and by blocking an enzyme peptidestransferase [1 - 3].

For this reason, the aim of this study was to investigate the in vitro effect of selected physicochemical factors on the adsorption capacity of different types of chitosan and evaluation of the assumption that the use of chitosan formulations is essential for the bioavailability of ingested simultaneously orally administered drug substance and explanation of the mechanism of interaction of the drug (chloramphenicol) with nutritional supplements containing chitosan.

2. Materials and method

2.1. Materials

In the study natural chitosans was used with a high degree of deacetylation of from 85% to 95%, treated with IR radiation dose of from 5 to 30 kGy different manufacturers (***Table 1***, was presented in [4]. Chloramfenicol (Polfa Kraków SA, s. 20299, Poland).

2.2. Method

The phenomenon of adsorption of the drug were tested in the dynamic pharmaceutical model simulating the in vitro conditions. The amount of adsorbed drug by chitosan was calculated from the difference of tested concentrations formulations before and after the sorption. Tests were carried out spectrophotometrically at a wavelength of 273 nm (determined by the linear regression for chloramfenicol was $y = 29.359 x - 0.0034$ and $R^2 = 0.9966$ calculated),

2.3. Studies adsorption of chloramfenicol

The phenomenon of adsorption of chloramphenicol was examined by dynamic model in the concentration range of overall single dosage using a pharmaceutical model of gastrointestinal tract with modifications based on research by. Polish Pharmacopoeia for such formulations [1 - 8]. The study was performed in a shaking water bathmaintaining the conditions resembling as closely as possible the conditions existing in the gastrointestinal tract. Vibration amplitude was established (300 r.p.m.) and the process temperature (37 °C).

In to centrifuge vials containing 5 ml of 2 ml were metered suitable chitosans solution and adjusted to pH 2 (0.05 M HCl), which corresponds to the gastric pH in the fasting state. Volume of solution used corresponds to 0.03 g of chitosan (the dose used as a dietary slimming). Then the vial was added the corresponding amount of medicinal substance 0.05 g of chloramphenicol (in the dose of medicinal therapies) and shaken (300 r.p.m.) for 2 hours. The contents of the tubes was adjusted with 0.1 M Na_2CO_3 to pH 7.0 - 7.6, which corresponds to the pH of the intestinal tract and colon. The samples were incubated at 37 °C with shaking (300 r.p.m.) for 2.5 hours. Tested system was adjusted to room temperature and centrifuged in a centrifuge (2100×g) for 20 minutes, then was allowed to stabilize for about 0.5 hours. Then collected into clean tubes 1.5 ml of the supernatant solution and determined spectrophotometrically (λ = 273 nm) in a 1 cm quartz cuvettes.

3. Results and discusion

3.1. Effect of intrinsic viscosities and viscosity-average molecular weights for the adsorption process of chloramphenicol for chitosans

Analysis of dose-degrading effect on adsorption capacity of chloramphenicol for chitosans shows a pattern where the reduction of the intrinsic viscosity of the chitosan is noted the increasing the number of bonded drug ***Table 1*** and ***Figure 1***. Research of chitosan viscosity used in the work was carried out. The procedure described in previous work [7].

Table 1. *The value of essential intrinsic viscosity and chloramphenicol binding by various kinds of chitosan's in g/g in investigated chitosan's and chitosan preparations.*

Sample No.	Type of chitosan (Ionizing radiacion of kGy)	Intrinsic viscosity, dm^3g^{-1}	Average number of antibiotic bonded by 1 g of chitosan, g	Standard deviation DS, g	RDS relative standard deviation, %
1	Chito-Clear TM 1015 (0)	0,2852	1,504	0,035	4,36
2	Chito-Clear TM 1015 (5)	0,2545	1,466	0,044	3,98
3	Chito-Clear TM 1015 (10)	0,2282	1,312	0,057	4,34
4	Chito-Clear TM 1015 (15)	0,2057	1,308	0,011	3,24
5	Chito-Clear TM 1015 (20)	0,1872	1,244	0,048	3,86
6	Chito-Clear TM 1015 (30)	0,1576	1,196	0,024	4,12
7	Chitosan type 352 food grade (0)	0,2117	1,340	0,033	4,46
8	Chitosan type 352 food grade (5)	0,1949	1,252	0,037	4,34
9	Chitosan type 352 food grade (10)	0,1696	1,169	0,054	4,25
10	Chitosan type 352 food grade (15)	0,1639	1,093	0,050	3,87
11	Chitosan type 352 food grade (20)	0,1575	1,024	0,034	3,12
12	Chitosan type 352 food grade (30)	0,1497	0,931	0,022	2,36
13	Chitosan Huasu sample (0)	0,7437	0,750	0,023	3,06
14	Chitosan Huasu sample (5)	0,5843	0,717	0,037	2,61
15	Chitosan Huasu sample (10)	0,5185	0,549	0,014	4,01
16	Chitosan Huasu sample (15)	0,3717	0,437	0,028	4,03
17	Chitosan Huasu sample (20)	0,3303	0,423	0,010	4,48
18	Chitosan Huasu sample (30)	0,2986	0,371	0,026	4,69
19	Chromdiet®	0,1872	0,927	0,042	3,56
20	Bio-active®	0,1576	1,242	0,022	3,86
21	Witana®	0,1774	0,986	0,044	4,12

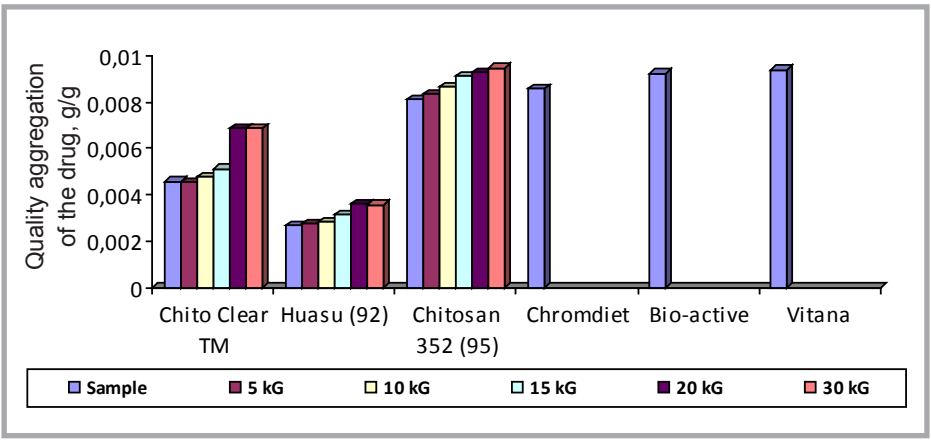

Figure 1. *Binding of Chloramfenicol by different types of chitosans according to the dose of radiation degrades in kG (temp. 37 °C and pH 7.6).*

Analysis of indications viscosity average molecular weights has shown that these values for the chitosans vary depending on the degree of degradation of the radiation of the polymer. The results show that chloramphenicol is adsorbed onto the chitosan pH ranges used, and the binding capacity varies with the type of chitosan and its degradation.

The measurement results of the adsorption process of chloramfenicol by chitosan contained in the co-administered preparations generally available for purchase handwritten confirmed the hypothesized that the adsorption is highly variable for different preparations. The strongest is bound by the preparation of Vitana®, and the least of the preparation Chromdiet®.

Binding of of chloramphenicol by the individual market slimming preparations show similar values, but is much greater in comparison to the adsorption of the drug by various chitosan manufacturers. Chitosan contained in the medicinal formulations have the ability to bind close to 100% of the dose, and thus significantly effect on the bioavailability of the concomitant chloramphenicol.

The fact of the lowest value of adsorption at pH 6.4 can be explained by the chemical properties of chitosan, which has a charge only at pH > 6.7, and the electrostatic adsorption can exhibit in relation to medicinal substances [7, 8].

At a pH above 7.6 corresponding to the environment of the gut filled ingest, the average size of the sorption for the highest dose of the chitosan was in the range 22.30% to 100.00%.

4. Conclusion

The increase size of polymer adsorption chloramphenicol with increasing pH from 7.6 to 8.0 can be explained by swelling properties of chitosan that forms conglomerate present in the form of the emulsion system.

Based on the above considerations it can be concluded that, between the test drug and the polymer is an antagonist interaction consisting of the adsorption of the drug on the polymer which is chitosan, which reduces its bioavailability and therapeutic concentration.

5. References

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