THE ROLE OF HALOIDS (BROMINE AND IODINE) IN THE METAMORPHOSIS OF AMPHIBIA

O.A. Krylov

The Laboratory of Comparative Ontogenesis of the Nervous System (Head-Prof. A.A. Volokhov) of the Institute of Normal and Pathological Physiology (Dir.-Active Member of the AMN SSSR V.N. Chernigovskii) Akad. Med. Nauk SSSR, Moscow

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The ideas of several authors [5,14] on the special role of the hypophysis in the metabolism of bromine and the formation of the bromine hormone in the hypophysis has, at the present time as well as earlier [8], given rise to considerable doubts. Numerous investigations [2,3,4,11,12,13,16,17,19,20,22], using the method of tagged atoms, have conclusively shown that the only site of accumulation of bromine in the organism is the thyroid gland, and that only there can bromine be detected in the composition of the protein. These data obtained in relation to bromine have long been known in regard to iodine. However, if the role of iodine in the function of the thyroid gland is more or less known, then this cannot be said of bromine, despite the fact that in several investigations [7,8,9] a relationship has been pointed out between the histogenesis of the thyroid gland and the introduction of external bromine.

As is well known, one of the most sensitive indicators of the activity of thyroid gland hormones is the metamorphosis of amphibia. The ideal subject in this case is the axolotl (the neotonic form of Amblystoma mexicanum), since the axolotl, under natural conditions, does not possess the capacity of independent metamorphosis. Thus, any indications of the conversion of the axolotl to its adult form—amblystoma – must be regarded as a result of the experimental activity [6].

The purpose of the present work was to compare whatever influence bromine and iodine showed on the metamorphosis of the axolotls.

EXPERIMENTAL METHOD

We used 52 axolotls in the experiment, 8-10 months of age (of these, 40 axolotls were of the black race, and 12 white), drawn from the eggs of one laying.

Two series of experiments were carried out on 20 axolotls, which had been transferred to 4 aquariums, 5 in each. The third series included 12 axolotls, transferred to 4 aquariums, 3 in each. In the aquariums the animals found themselves under conditions of constant temperature and lighting and the same amount of water. In all the aquariums thyroidin was added in dilution, the concentration being 0.01 g/l in two of the series and 0.075 g/l in one. In one of the aquariums sodium bromide was added in addition to thyroidin (0.05% solution of NaBr), in another, sodium iodide (0.05% solution of NaI), and in a third, both sodium bromide and sodium iodide, each salt in a concentration of 0.025% so that together the total concentration of the two salts equalled 0.05%. The animals in the fourth aquarium, in which only thyroidin was dissolved, served as the control.

During the process of metamorphosis each axolotl was systematically noted for weight, gill length, width of tail, color, and time when it crawled out into dry land and transferred to lung breathing. These data were able to illustrate one or another effect of each of the haloids on the dynamics and rapidity of the metamorphosis.

EXPERIMENTAL RESULTS

In all three series of experiments we obtained identical results. The most characteristic trials are presented in the graphs in Fig. 1, showing the dynamics of the changes (per day) in the gill length, width of the caudal fin, and weight of the animals.

In the control animals that were only subjected to the effects of thyroidin only, minimal changes were observed during the first 20-25 days in the gill length, width of the tail, and weight; on the curve this is manifested in the form of a peculiar "plateau", most clearly expressed in relation to the changes in gill length (see Fig. 1, A). Following this "plateau", the curves trace a marked shift for all the criteria noted above, and on the 35-50th day the metamorphosis of the axolotl converts it from the larval to the adult form – the amblystoma.

In the experiments on the effect of sodium bromide on the axolotls in addition to thyroidin, the metamorphosis ran a different course. The "plateau" which was

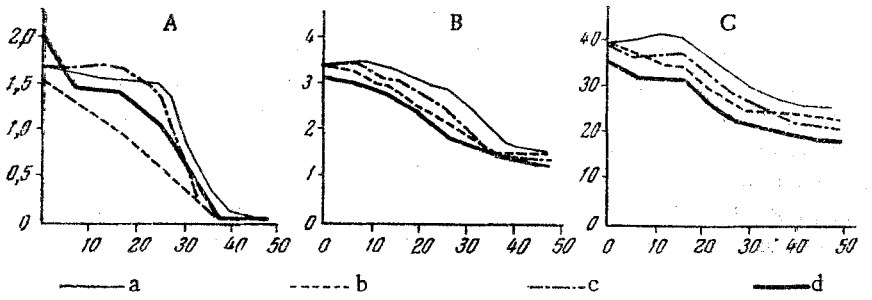

Fig. 1. Changes in the gill length (A), width of the caudal fin (B), and weight (C) of the individual axolotls under the influence of thyroidin (control), and the simultaneous effects of the salts of iodine and bromine. Concentration of thyroidin 1:100,000. On the ordinate axis – gill length in centimeters (A); height of the caudal fin in centimeters (B); weight of the axolotl in grams (C); on the abscissa axis – duration of the metamorphosis (in days); a) Control; b) NaBr; c) NaI; d) NaBr, NaI.

observed in the control animals here either completely disappeared or remained poorly noted. Thus, the effect of bromine appears to be mainly on the first stages of the metamorphosis.

Under the conditions testing the effect of sodium iodide, the "plateau", although also decreasing, did so very minimally in comparison with that which was observed in the control experiments; in addition, in several experiments there was even noted an increase in the gill length and other indicators during the first days of the metamorphosis.

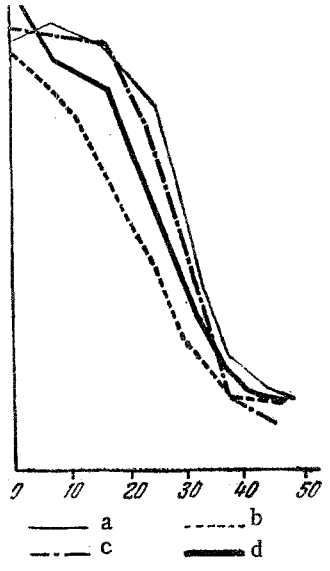

Fig. 2. The general "metamorphosis curve", occuring under different conditions, according to the criteria of gill length, height of the caudal fin, and weight of the animal. Symbols are the same as in Fig. 1.

The experiments with the simultaneous actions of the salts of bromine and iodine on the metamorphosis of the axolotls also showed a disappearance of the "plateau" observed in the control animals, although here this phenomenon was manifested to a somewhat lesser degree than in the experiments with the action of bromine alone.

If, on the basis of all the criteria of metamorphosis selected by us (changes in the gill length, width of the caudal fin, and weight), one general curve, arbitrarily called the "metamorphosis curve", is traced for each animal, then it is possible to clearly see the inferences noted above (Fig. 2).

At a concentration of 0.01 g/l of thyroidin the metamorphosis of the axolotls exposed to the action of either the bromine or iodine salts, as well as to their joint activity, was completed 5-10 days earlier than in the control animals (Fig. 3).

At higher concentrations of thyroidin (0.075 g/l) this difference was less manifest. On the average, the duration of metamorphosis of the control axolotls was greater than the duration of metamorphosis of the axolotls subjected to the action of haloids by 3-7 days (see table).

Statistical analysis of the material showed the obtained difference to be significant. We were not successful in detecting a significant difference in the rapidity of the metamorphosis within a comparison of the data from the experiments with bromine, iodine, and their conjoint activity.

Following the completion of metamorphosis several of the animals died. The largest number of axolotls died in the experiments with the action of the iodine salt (11 animals), a smaller number in association with the action of the bromine salt (8 animals), still fewer with the conjoint action of the salts of bromine and iodine (5 animals), and the fewest – in the control experiments (3 animals).

From this one may postulate that iodine possesses a greater toxicity than bromine. The simultaneous

action of the bromine and iodine salts probably, to some degree, neutralized their toxicity, although their total concentration, as we already noted, was the same as in the experiments using either one of the salts. One can consider that bromine and iodine act on different phases of the metabolism, and, thus, their joined effect was less toxic than in those cases where either one of the haloids acted alone.

As is well known, iodine is necessary for the construction of the active portion of the thyroid gland hormone – thyroxin – and as far as this is concerned the mechanism of action of iodine is more or less clear. In regard to bromine, here great investigative work is still needed for a concrete answer.

According to the data in the literature [4,7], microdoses of bromine show a stimulatory effect on the thyroid gland, manifested by its hyperplasia, augmentation of the secretory activity of the epithelium, and the accumulation of colloid within it. It is interesting that the thyroid gland of the animals subjected to the action of bromine shows a stronger influence on the metamorphosis of the amphibia than the gland of the intact animals [7]. At the same time, basal metabolism, under the influence of bromine, either does not change or decreases. In addition, the accumulation of iodine by the thyroid gland is shown to be considerably decreased [4].

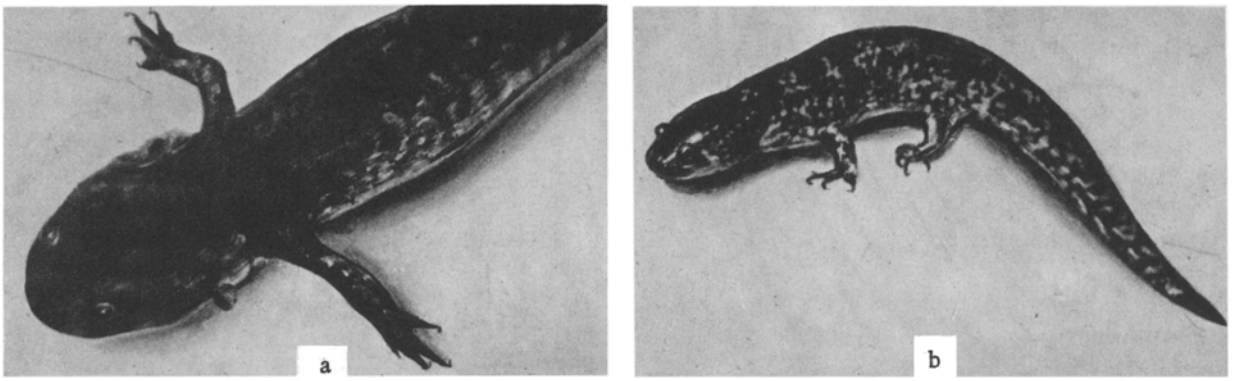

Fig. 3. Conversion of the axolotl to an amblystoma with the action of thyroidin (a) and the simultaneous action of thyroidin and sodium bromide (b) on the 49th day of metamorphosis.

The experimental material of the present work and the data in the literature compel postulation that bromine derivatives of the thyroid gland stimulate the metamorphogenic conversion of the so-called mucigenous protein to a more highly differentiated "dry protein", that being graphically displayed in the metamorphosis of the amphibia although the same process, obviously, occurs in all vertebrate animals.

Thus, bromine may be regarded as a synergist of iodine in its participation in the process of metamorphogenic conversion of the protein, and as a relative antagonist to the accumulation of iodine in the thyroid gland and in its participation in the processes of basal metabolism. On the strength of the close chemical relationship of bromine and iodine, the former can, in a number of instances, take the place of iodine in the thyroxin molecule or the amino acids participating in its structure. It is known that compounds such as these are encountered in nature [15,18], and may be obtained artificially [21].

Thus, it may be postulated that one of the means of action of bromine on the organism via the thyroid gland is the replacement of the atoms of iodine in thyroxin by atoms of bromine, so that the effectiveness of the hormone's action, and, possibly, even the character of its action, is determined by the number of replaced atoms.

SUMMARY

The author compared the effect of bromine and iodine on metamorphosis of Amblystoma mexicanum. 52 axolotls were subjected to the action of thyroidin (0.01) and haloid salts: 0.05% NaI solution in the second, 0.025% NaBr and 0.25% NaI in the third and fourth series of experiments. Apart from thyroidin no other additional salts were introduced.

As shown, during thyroidin action bromine and iodine salts tend to accelerate the metamorphosis of A. mexicanum, by 5-10 days. Bromides exert a higher effect on the primary metamorphosis stages. Because of these, the dynamics of metamorphosis under the effect of bromides differs from that under the action of iodides. A suggestion is made that brimine participates in the thyroid gland function.

Control	0.05% NaBr	0.05% NaI	0.025% NaBr 0.025% NaI
Thyroidin in a concentration of 0.01 g/1			
50	30	35	40
50	30	40	35
40	45	40	45
40	35	35	35
45	40	40	35
50	30	42	30
50	40	40	40
50	45	45	30
Thyroidin in a concentration of 0.75 g/1			
35	30	30	32
32	30	30	35
35	32	30	35
35	30	32	35
35	30	32	35
Total average value			
42±2,2	34±1,8	36±1,7	36±1,5
Average for the experiments with thyroidin in a concentration of 0.01 g/1			
47±1,8	37±2,5	40±1,5	36±2,0

Rapidity of the Metamorphosis of Axolotls Under the Influence of Thyroidin and Salts of Bromine and Iodine (in days)

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