# Renal Transport of Urea and Some Carbohydrates in *Lophius piscatorius*[1]

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The renal handling of urea has been studied by many investigators on a host of animals. It has been found that urea is actively secreted by certain species (Munro, '53; Forster, '54), reabsorbed by others (Smith, '31a, b), and in some the renal handling seems to be entirely passive (Shannen, '36). The aglomerular goose fish (*Lophius piscatorius*) is reportedly able to secrete urea actively from peritibular blood into the tubular urine (Schmidt-Nielson, '51; Smith, '51). This conclusion is based upon the observation by Grafflin (Grafflin, '36) that after exogeneous urea was injected intramuscularly into goose fish, the U/P ratios for urea were appreciably above one. However, Grifflin pointed out that when endogenous urea was considered, the U/P ratios were equal to or less than one. Grafflin recognized that without any information on water reabsorption it was impossible to determine if U/P ratios above 1.0 resulted from secretion or from passive concentration due to water removal. Interpretation of these experiments is further complicated by technical considerations. Because Grafflin injected urea intramuscularly into the tail of the goose fish, blood perfusing the kidneys would have had a high concentration of urea relative to that in mixed venous or arterial blood, since the goose fish kidney is supplied almost entirely by venous blood which has been derived from the caudal portions of the animal. It is apparent that the systemic blood urea concentration of *Lophius* under these conditions would be lower than that existing in blood perfusing the renal tubules, and would continue to be lower until all injected urea is absorbed from the muscles in the tail. Since Grafflin obtained blood samples from either the heart or from the mixed venous pool, the analyzed blood urea concentration values were lower than those actually existing in blood perfusing the kidneys. Consequently, he would have calculated erroneously high U/P ratios, leading to the conclusion of an apparent urea secretion. The present study was undertaken to determine whether in fact the goose fish secrete urea, or whether the findings of apparent urea secretion result from the experimental technique used by Grafflin. In addition we have studied the rate of entry of arabinose and fructose into goose fish urine.

## METHODS

All the goose fish used in this study were taken by drag net in the vicinity of the Mount Desert Island Biological Laboratory. The fish upon capture were immediately placed in large buckets of running sea water and remained there until the dragger returned to dock on the same day. The fish were immediately transported back to the laboratory where they were kept in tubs of running sea water, and work was begun on the fish within the next two-three hours. Thus, all fish were used for experiments between 6–12 hours after capture by the drag.

A polyethylene catheter was inserted into the urinary papilla and tied securely. At the beginning of each experiment the bladder was flushed out by pressure on the ventral surface of the fish, and the urinary catheter was then sealed. Urine collections were taken at timed intervals by simply opening the ureteral catheter, and pressing on the ventral surface of the fish until urine ceased to empty out of the catheter. Air was then blown into the

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bladder and pressure again applied to the ventral surface to make sure that all urine was emptied from the bladder. At the end of each collection the ureteral catheter was resealed for the next collection period. At the beginning and end of each collection period, blood was drawn from a vertebral artery or vein. The average of these two blood samples was taken as the average plasma value for that period and used to compute the U/P ratios. Urea in one series of experiments was injected intramuscularly in the tail. In another series of experiments, urea was injected both intramuscularly and subcutaneously in the head region. In this second series of experiments it was presumed that the mixed venous blood would have the same concentration of urea as blood perfusing the kidney, since blood passing through the site of injection first went to the heart before it went to the kidney. Arabinose and fructose were injected as in the latter urea experiments.

The following chemical methods were used: urea, Conway micro diffusion tech-

TABLE 1

*Protocol of an experiment in which urea was injected IM in the tail*

| Time in minutes | Urine volume | Urea concentration μM/ml | | U/P ratio |
|---|---|---|---|---|
| | | Urine | Plasma mid points | |
| | *ml/hr.* | | | |
| 0 | Inject 7.5 gm urea in 15 ml $H_2O$ intramuscularly in tail | | | |
| 10–123 | 1.0 | 130 | 80.7 | 1.61 |
| 123–178 | 1.4 | 103 | 89.5 | 1.15 |
| 178–252 | 1.2 | 104 | 102.0 | 1.02 |
| 252–314 | 1.5 | 113 | 92.5 | 1.22 |
| 432–604 | 1.5 | 107 | 93.0 | 1.15 |
| 604–834 | 1.3 | 101 | 91.7 | 1.10 |
| 834–1549 | 1.05 | 86 | 87.8 | 0.98 |
| 1549–2029 | 1.2 | 80 | 86.0 | 0.93 |

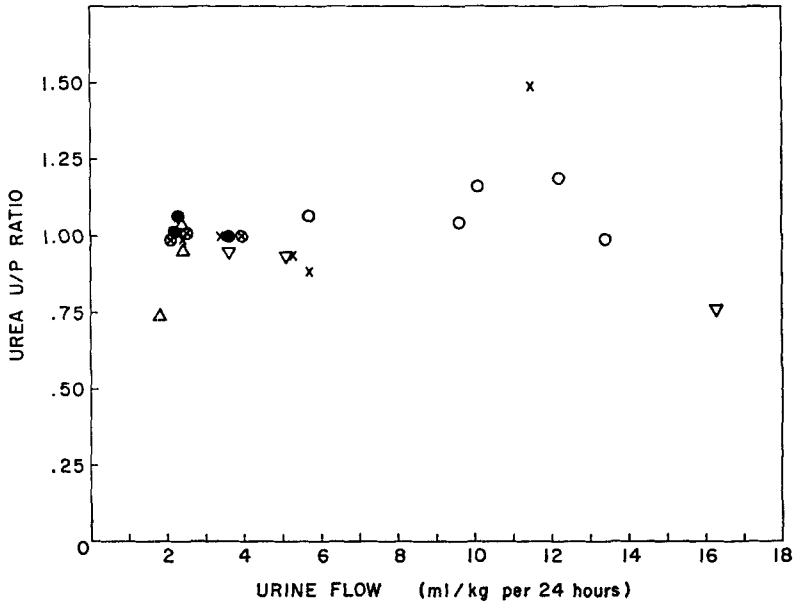


Fig. 1 Independence of U/P ratios for urea and urine flow. Each symbol represents a different fish.

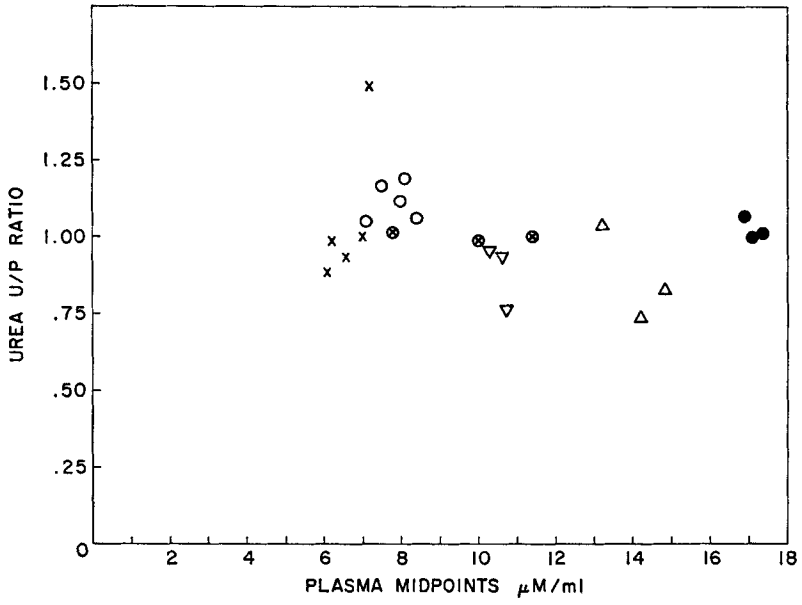


Fig. 2 Independence of U/P ratios for urea and plasma concentration of urea. Each symbol represents a different fish.

nique (Conway, '42); arabinose, Roe and Rice ('48); fructose, Schreiner ('50).

## RESULTS

*Urea.* Table 1 is the protocol of an experiment in which urea was injected intramuscularly in the tail region. The apparent U/P ratios for urea were considerably above one in the first few urine collection periods, fell slightly with each succeeding period, and approached unity during periods 7 and 8. It was this experiment which initially suggested that high urea U/P ratios seen by other workers were not the result of active urea secretion by the goose fish kidney, but rather were an experimental artifact. Accordingly, a second series of experiments was performed in which urea was injected intramuscularly and subcutaneously into the head region instead of the tail. Urinary collections were generally not begun until 10–12 hours after the time of injection so that urea concentrations in plasma were maintained relatively constant during the entire experiment. Results from a total of 22 collections obtained from 6 different fish are plotted in figures 1 and 2. When urea U/P ratios calculated from urea concentrations in mEq/kg of water are plotted against urine flow, it is found that the U/P ratio is essentially one over the entire range of urine flows studied (fig. 1). Data presented in figure 2 indicate the absence of any relationship between plasma urea concentration and U/P urea values, the average of which was 1.01 ± a standard error of 0.03. It is therefore apparent that

TABLE 2

*Summary of results showing U/P ratios for D-arabinose, L-arabinose and fructose*

| | Average U/P ratio | Standard deviation | Number of collection periods | Number of fish | Range of plasma concentration in μM/ml |
|---|---|---|---|---|---|
| L-arabinose | 0.126 | 0.055 | 28 | 7 | 3.97–11.7 |
| D-arabinose | 0.194 | 0.066 | 16 | 4 | 2.9 –15.0 |
| Fructose | 0.081 | 0.028 | 6 | 2 | 8.3 –14.7 |

the U/P urea ratio was independent of both plasma urea concentration and rate of urine flow.

*Arabinose.* In other experiments D-arabinose, L-arabinose or fructose was injected intramuscularly and subcutaneously in the head region. In all collection periods of all animals studied, these sugars appeared in the urine (table 2). The average U/P ratio for fructose was lowest and that for D-arabinose highest. All the U/P ratios showed a statistically significant difference from each other, with the P values for any pair being less than 0.01.

## DISCUSSION

Our experiments offer no evidence for postulating active urea transport by the kidney of the goose fish. Only in those experiments in which urea was injected in the tail were urea U/P ratios significantly above one in the first few collection periods. When the bolus of injected urea was absorbed completely, so that there would be no difference between the concentration of urea in the mixed venous blood and the concentration in the blood going to the kidney, the U/P ratios approached unity. In experiments in which urea was injected in the head region, the U/P ratios for urea were uniformly around one under all conditions tested. We feel, therefore, that it is unlikely that the goose fish kidney can actively transport urea against a chemical gradient.

The finding that both 5 and 6 carbon atom sugars were capable of entering the urine was at first surprising since others had reported that only "trace" amounts are able to cross the tubular epithelium (Smith, '51; Marshall, '34). Some workers reported that neither xylose nor glucose appears in the urine (Jolliffe, '30; Marshall and Grafflin, '28). However, subsequent investigators, using more refined analytical methods have shown that both xylose and glucose can be detected in the urine (Clarke and Smith, '32; Marshall, '30).

Our results clearly show that sugars are capable of diffusing across the nephron. The site and mechanism of transport are unknown. The sugars may simply have diffused across the renal tubular cells passively along a chemical gradient, or may have moved by exchange diffusion backwards across an existing transport system. Although we are unable to determine which mode of entry was responsible for the appearance of fructose in the urine, we feel that arabinose transport probably resulted from passive diffusion. It is known that several types of cells contain a transport system which permits rapid entry of L-arabinose but which tends to exclude D-arabinose (Crane, Field and Cori, '57; Segal, Wyngaarden and Foley, '57; Le Fevre and Marshall, '58). Our data indicate the absence of such a system in tubular epithelium of *Lophius*, suggesting that both D and L-arabinose simply leaked through non-specific pores from blood into the lumen.

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