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Effects of Dietary Bile Acid Supplementation Levels on Growth Performance, Morphological Indices, and Body Composition of Juvenile Schizothorax prenanti Postprint

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Abstract

This study was conducted to investigate the effects of dietary bile acid supplementation levels on growth performance, morphometric indices, and body composition of juvenile Schizothorax prenanti. Three hundred sixty healthy juvenile Schizothorax prenanti with an average body weight of (12.74±0.14) g were randomly allocated into four groups with three replicates per group and 30 fish per replicate. The four groups were fed experimental diets supplemented with 0 (control), 75, 150, and 300 mg/kg bile acids for 70 days. The results indicated that with increasing bile acid supplementation levels, weight gain rate (WGR), specific growth rate (SGR), and protein efficiency ratio (PER) of juvenile Schizothorax prenanti exhibited an initial increase followed by stabilization, whereas feed conversion ratio (FCR) showed an initial decrease followed by stabilization. The WGR, SGR, and PER in all bile acid-supplemented groups were significantly higher than those in the control group ($P<0.05$), while FCR was significantly lower than that in the control group ($P<0.05$). WGR and SGR reached maximum values of 226.63% and 1.69%/d, respectively, at a bile acid supplementation level of 150 mg/kg; PER attained a maximum value of 1.64% at 300 mg/kg; and FCR reached a minimum value of 1.56 at 75 mg/kg. Quadratic regression analysis revealed that the optimal bile acid supplementation levels for WGR, SGR, PER, and FCR were 186.83, 192.86, 166.67, and 183.33 mg/kg, respectively. With increasing bile acid supplementation levels, condition factor (CF) of juvenile Schizothorax prenanti exhibited an initial increase followed by stabilization, while viscerosomatic index (VSI) and hepatosomatic index (HSI) showed initial decreases followed by stabilization. CF in all bile acid-supplemented groups was significantly higher than that in the control group ($P<0.05$), whereas VSI and HSI were significantly lower than those in the control group (P<0.05). With increasing bile acid supplementation levels, crude protein content in whole fish and muscle of Schizothorax prenanti exhibited an initial increase followed by stabilization, while crude lipid content in whole fish, muscle, and hepatopancreas showed an initial decrease followed by stabilization; however, moisture and crude ash contents in whole fish and muscle showed no significant changes (P>0.05). It can be concluded that dietary bile acid supplementation can effectively improve feed utilization efficiency, promote growth, enhance morphometric indices, and reduce lipid deposition in muscle and liver of juvenile Schizothorax prenanti. Based on comprehensive consideration, the appropriate dietary bile acid supplementation level for Schizothorax prenanti is 166.67-192.86 mg/kg.

Full Text

Abstract

This experiment was conducted to investigate the effects of dietary bile acid supplementation levels on growth performance, physical indices, and body composition of juvenile Schizothorax prenanti. A total of 360 healthy juvenile fish with an average body weight of (12.74±0.14) g were randomly divided into four groups with three replicates each (30 fish per replicate). The four groups were fed experimental diets supplemented with 0 (control), 75, 150, or 300 mg/kg bile acid for 70 days. The results showed that as bile acid supplementation increased, weight gain rate (WGR), specific growth rate (SGR), and protein efficiency ratio (PER) initially increased then plateaued, while feed conversion ratio (FCR) initially decreased then stabilized. All bile acid supplementation groups exhibited significantly higher WGR, SGR, and PER compared to the control group (P<0.05), while FCR was significantly lower (P<0.05). Maximum WGR and SGR (226.63% and 1.69%/d, respectively) occurred at 150 mg/kg bile acid, whereas maximum PER (1.64%) occurred at 300 mg/kg. Minimum FCR (1.56) was observed at 75 mg/kg. Quadratic regression analysis indicated that optimal bile acid supplementation levels for WGR, SGR, PER, and FCR were 186.83, 192.86, 166.67, and 183.33 mg/kg, respectively. Condition factor (CF) followed a similar increasing-then-plateauing trend, while viscerasomatic index (VSI) and hepatosomatic index (HSI) decreased then stabilized with increasing bile acid levels. CF in all supplemented groups was significantly higher than the control (P<0.05), whereas VSI and HSI were significantly lower (P<0.05). Whole-body and muscle crude protein content increased then plateaued with bile acid supplementation, while crude lipid content in whole body, muscle, and hepatopancreas decreased then stabilized. Moisture and ash content in whole body and muscle showed no significant changes (P>0.05). These results demonstrate that dietary bile acid supplementation effectively improves feed utilization, promotes growth, enhances physical indices, and reduces lipid deposition in muscle and liver of juvenile S. prenanti. Based on comprehensive evaluation, the appropriate bile acid supplementation level in diets for this species ranges from 166.67 to 192.86 mg/kg.

Keywords: Schizothorax prenanti; bile acid; growth performance; physical indices; body composition

Introduction

Schizothorax prenanti is a benthic cold-water fish species native to the upper Yangtze River, valued for its tender flesh, rich nutritional content, and delicate flavor [1]. It represents an important economic fish species in China. In recent years, S. prenanti aquaculture has developed rapidly with increasing production volumes. However, under intensive culture conditions, farmers often use high-lipid compound feeds to accelerate growth, resulting in excessive body fat accumulation. This not only reduces flesh quality and edible portion ratio but also wastes feed nutrients and increases production costs. Therefore, promoting lipid catabolism and improving protein deposition in S. prenanti has become an urgent challenge.

Bile acids are major components of bile that play crucial roles in animal lipid metabolism. Their molecular structure features a lipophilic alkyl group at one end and hydrophilic hydroxyl and carboxyl groups at the other, conferring strong surface activity that reduces interfacial tension between oil and water phases. This property promotes fat emulsification, forming fatty acid chylomicrons that remain suspended in water and expanding the contact area between lipids and lipases, thereby accelerating fat digestion and absorption and improving lipid digestibility. This emulsifying action also enhances absorption and utilization of other nutrients, particularly fat-soluble vitamins, carotenoids, and trace elements [2], while improving growth performance and providing antimicrobial and immunity-enhancing effects [3].

Reinhart et al. [4] found that bile acids significantly increased feed intake, weight gain, fat intake, and nitrogen retention in weaned piglets. Pullen et al. [5] demonstrated that bile acids improved fat digestion and absorption in broiler chickens. In fish, bile acids promote growth, reduce body fat deposition, and increase edible portion ratio [6-8], though related research remains limited. This study investigates the effects of different dietary bile acid levels on growth performance, physical indices, and body composition of S. prenanti to provide theoretical reference for bile acid application in compound feeds for this species.

1.1 Experimental Diets

A basal diet was formulated using fish meal, soybean meal, and rapeseed meal as protein sources, soybean oil as lipid source, and -starch and wheat middling as carbohydrate sources. Bile acid (provided by Guangzhou Xintun Aquatic Technology Co., Ltd., containing 15% active ingredients, primarily hyodeoxycholic acid and lithocholic acid) was supplemented at 0, 75, 150, or 300 mg/kg to create four isonitrogenous and isolipidic experimental diets. All ingredients were ground to pass through a 60-mesh sieve, weighed, and thoroughly mixed. Minor components were incorporated using the progressive enlargement method.

The mixture was processed into 1 mm diameter pellets using a laboratory meat grinder, air-dried, and stored at -20°C until use. The basal diet composition and nutrient levels are presented in Table 1 .

1.2 Experimental Design and Management

Juvenile S. prenanti were purchased from Ya' an Cold-Water Fish Farm as a single batch of offspring. After transportation, fish were disinfected with 4% salt solution and acclimated in holding tanks, where they were fed the basal diet to satiation to adapt to experimental conditions and feed. Following a 7-day acclimation period, 360 healthy fish with uniform size, weighing (12.74±0.14) g, were randomly allocated into four groups (one control and three treatment groups) with three replicates each (30 fish per replicate). Fish were randomly distributed among 12 experimental aquaria (1.06 m × 0.41 m × 0.38 m) by replicate. The control group received the basal diet without bile acid, while treatment groups received diets supplemented with 75, 150, or 300 mg/kg bile acid for 70 days. During the trial, fish were hand-fed to apparent satiation three times daily (08:00, 13:00, 16:00). Tanks maintained a micro-flow water system with 30% daily water exchange. Water temperature, feeding behavior, and mortality were monitored daily. Water temperature was maintained at 15-20°C, dissolved oxygen remained above 6.0 mg/L, and pH ranged from 7.0 to 7.5.

1.3 Sample Collection

At the end of the trial, fish were fasted for 24 h before counting and weighing each replicate. Five fish per replicate were anesthetized with 50 mg/L MS-222 solution, measured for body length and weight, then dissected to obtain viscera, hepatopancreas, and adipose tissue for calculating hepatosomatic and viscerasomatic indices and analyzing hepatopancreas nutrient composition. Dorsal muscle samples (below the dorsal fin and above the lateral line) were collected, sealed in self-sealing bags, and stored at -20°C for muscle nutrient analysis. Additionally, five fish per replicate were stored at -20°C for whole-body nutrient analysis.

1.4 Index Determination

Moisture, crude protein, crude lipid, and ash contents in diets, whole body, muscle, and hepatopancreas were determined according to AOAC (1995) [9] methods. Crude protein was measured by the Kjeldahl method, crude lipid by Soxhlet extraction (using ether), moisture by oven drying at 105°C, and ash by combustion at 550°C.

1.5 Calculation Formulas

Weight gain rate (WGR, %) = $100 \times (W_t - W_0) / W_0$
Specific growth rate (SGR, %/d) = $100 \times (\ln W_t - \ln W_0) / t$

Protein efficiency ratio (PER, %) = (Wt - W0) / (F × P)
Feed conversion ratio (FCR) = F / (Wt - W0)
Survival rate (SR, %) = 100 × Nf / Ni
Condition factor (CF, g/cm^3) = Wt / L^3
Viscerasomatic index (VSI, %) = 100 × Wv / Wt
Hepatosomatic index (HSI, %) = 100 × Wh / Wt

Where: W0 = initial body weight (g); Wt = final body weight (g); F = feed intake (g); P = dietary crude protein content (%); Ni = initial fish number; Nf = final fish number; t = feeding trial duration (d); L = body length (cm); Wv = viscera weight (g); Wh = hepatopancreas weight (g).

1.6 Statistical Analysis

Results are expressed as "mean ± standard deviation." Data were analyzed using one-way ANOVA with SPSS 19.0 software. When significant differences were detected, Duncan' s multiple comparison test was applied with significance level at $P < 0.05$. Quadratic polynomial regression was used to model relationships between WGR, SGR, PER, FCR and bile acid supplementation levels.

2 Results and Analysis

2.1 Effects of Dietary Bile Acid Level on Growth Performance of Juvenile S. prenanti

As shown in Table 2 , WGR, SGR, and PER of juvenile S. prenanti increased initially then plateaued with increasing bile acid supplementation. Maximum WGR and SGR (226.63% and 1.69%/d, respectively) occurred at 150 mg/kg bile acid, representing 29.95% and 17.36% improvements over the control group ($P < 0.05$). PER reached its maximum (1.64%) at both 75 and 300 mg/kg bile acid, an 8.44% increase compared to the control ($P < 0.05$). When bile acid supplementation reached 75 mg/kg, no significant differences were observed among treatment groups for WGR, SGR, or PER ($P > 0.05$), though all remained significantly higher than the control ($P < 0.05$). FCR decreased initially then stabilized with increasing bile acid levels, reaching its minimum (1.56) at 300 mg/kg, a 6.59% reduction from the control ($P < 0.05$). At supplementation levels 75 mg/kg, FCR values did not differ significantly among treatment groups ($P > 0.05$) but remained significantly lower than the control ($P < 0.05$).

Quadratic polynomial regression analysis (Fig. 1 [Figure 1: see original paper]~4) revealed the following relationships: WGR (y) = $-0.0015x^2 + 0.5605x + 173.2$ ($R^2 = 0.9874$); SGR (y) = $-7\text{E-}06x^2 + 0.0027x + 1.4365$ ($R^2 = 0.9953$); PER (y) = $-0.0003x^2 + 0.1058x + 154.91$ ($R^2 = 0.8335$). Maximum values occurred at bile acid levels of 186.83, 192.86, and 166.67 mg/kg, respectively. The FCR regression equation (y) = $3\text{E-}06x^2 - 0.0011x + 1.6615$ ($R^2 = 0.8918$) indicated minimum FCR at 183.33 mg/kg bile acid. Survival rate was not significantly affected by bile acid supplementation ($P > 0.05$).

2.2 Effects of Dietary Bile Acid Level on Physical Indices of Juvenile S. prenanti

Table 3 shows that condition factor (CF) increased initially then plateaued with rising bile acid levels, peaking at 150 mg/kg (0.92 g/cm³). This value did not differ significantly from the 75 and 300 mg/kg groups ($P > 0.05$) but was significantly higher than the control ($P < 0.05$). Both viscerasomatic index (VSI) and hepatosomatic index (HSI) decreased then stabilized with increasing bile acid supplementation. At 75-300 mg/kg bile acid, VSI and HSI did not differ significantly among treatment groups ($P > 0.05$) but were all significantly lower than the control ($P < 0.05$).

2.3 Effects of Dietary Bile Acid Level on Body Composition of Juvenile S. prenanti

As shown in Table 4 , whole-body and muscle crude protein content increased initially then plateaued with bile acid supplementation, reaching maximum values at 150 mg/kg (12.68% and 15.44%, respectively). No significant differences were observed among supplemented groups (75-300 mg/kg) ($P > 0.05$), though all were significantly higher than the control ($P < 0.05$). Hepatopancreas crude protein showed no clear relationship with bile acid level and did not differ significantly among groups ($P > 0.05$). Crude lipid content in whole body, muscle, and hepatopancreas decreased then stabilized with increasing bile acid levels, with no significant differences among supplemented groups at 75-150 mg/kg ($P > 0.05$), though all were significantly lower than the control ($P < 0.05$). Moisture and ash contents in whole body and muscle, as well as moisture in hepatopancreas, did not differ significantly among groups ($P > 0.05$).

3 Discussion

3.1 Effects of Dietary Bile Acid Level on Growth Performance of Juvenile S. prenanti

Bile acids emulsify lipids, expanding the contact area with lipases and promoting lipid digestion and absorption, thereby improving dietary lipid utilization in fish [10]. Previous studies have demonstrated that dietary bile acid supplementation effectively enhances growth in bullfrogs (Rana catesbeiana), with optimal WGR, SGR, feed efficiency, PER, and nitrogen retention at 200 mg/kg [11]. Bile acid levels above 0.03% significantly improved WGR and feed utilization in cobia (Rachycentron canadum) [8], while ursodeoxycholic acid enhanced WGR and feed efficiency in yellowtail (Seriola quinqueradiata) [12]. Similarly, bile acid supplementation significantly increased SGR and PER while reducing FCR in juvenile turbot (Scophthalmus maximus) [13]. In this study, bile acid supplementation improved WGR, SGR, and PER while decreasing FCR in S. prenanti, with all parameters showing quadratic relationships with supplementation level. Quadratic regression analysis suggested that bile acid levels of 166.67-192.86 mg/kg optimize growth performance and feed efficiency, consistent with findings in Japanese eel (Anguilla japonica) [14], rainbow trout (Oncorhynchus mykiss) [15], and gibel carp (Carassius auratus gibelio) [16-17].

Potential mechanisms for bile acid' s growth-promoting effects include: (1) enhanced lipid emulsification and utilization, (2) increased digestive enzyme activity and activation of inactive lipase precursors in the intestine [18], and (3) antimicrobial properties that improve intestinal health and nutrient absorption [18]. Studies have shown that bile acids significantly increase lipase activity in Japanese flounder (Paralichthys olivaceus) [19], Japanese eel [14], and bullfrogs [11], promoting lipid digestion and metabolism. Additionally, bile acids can improve intestinal protease activity and apparent digestibility of dry matter, crude protein, and crude lipid, thereby enhancing feed conversion and growth [11]. However, Wang [7] found that bile acid supplementation significantly reduced FCR but did not affect WGR in giant freshwater prawn (Macrobrachium rosenbergii), suggesting that bile acid effects may vary with species, life stage, and dietary composition.

3.2 Effects of Dietary Bile Acid Level on Physical Indices of Juvenile S. prenanti

Viscerasomatic index (VSI) is primarily influenced by species and feeding conditions, while the liver serves as the main metabolic and nutrient storage organ in fish. Hepatosomatic index (HSI) at certain developmental stages reflects liver health status. Xiang et al. [20] suggested that VSI and HSI decrease as fish grow, as the body meets energy demands through improved feed conversion rather than increased organ size. Bile acids enhance conversion efficiency of dry matter and protein [11] and promote lipid utilization by regulating lipid metabolic enzyme activity [21], reducing energy deposition in viscera and increasing edible portion ratio. Huang et al. [22] reported that bile acid supplementation significantly increased hepatic lipase and lipoprotein lipase activities in turbot, enhancing hepatic lipid catabolism and providing hepatoprotective effects. In this study, VSI and HSI in all bile acid-supplemented groups were significantly lower than the control, with no significant differences among supplementation levels. However, Zhou et al. [8] found that bile acid increased HSI and VSI in cobia, while Hu et al. [11] reported reduced VSI but unchanged HSI in bullfrogs. Sun et al. [13] observed that VSI and intestinal somatic index in turbot increased then plateaued with bile acid supplementation, while VSI showed a gradual increasing trend. These discrepancies require further investigation.

Condition factor (CF) serves as a crude indicator of energy reserves and health status [23], reflecting nutritional condition [24]. Studies have shown that CF in cobia [8] and turbot [22] increased slightly with bile acid supplementation. In this study, CF in all supplemented groups was significantly higher than the control, with no significant differences among treatment groups, consistent with previous findings and indicating that bile acid improves feed utilization and promotes nutrient storage in S. prenanti.

3.3 Effects of Dietary Bile Acid Level on Body Composition of Juvenile S. prenanti

This study demonstrated that bile acid supplementation effectively reduced crude lipid content in whole body, muscle, and hepatopancreas while increasing crude protein content in whole body and muscle of juvenile S. prenanti, consistent with findings in cobia [8], turbot [13,22], and giant freshwater prawn [7]. These results suggest that bile acids promote lipid catabolism and enhance absorption and utilization of polyunsaturated fatty acids (PUFA) [7] to provide energy for metabolic activities. Additionally, bile acids facilitate binding of lipases to triglyceride droplet surfaces, increasing lipase activity and promoting lipid digestion [13]. Watanabe et al. [25] reported that bile acids activate G protein-coupled bile acid receptor (TGR5) on brown adipocyte surfaces in mice, increasing intracellular cAMP and thyroid hormone levels, accelerating basal metabolism, improving lipid transport, and reducing body fat content. Hu et al. [11] found that bile acids significantly increased nitrogen retention in bullfrogs, suggesting that bile acids spare dietary protein by promoting lipid catabolism, thereby enhancing protein deposition. Furthermore, reduced hepatic lipid deposition decreases the risk of fatty liver disease. These findings demonstrate that bile acid supplementation effectively improves body nutrient composition, reduces hepatic lipid accumulation, and prevents fatty liver development in fish.

Under the conditions of this study, dietary bile acid supplementation effectively improved feed utilization, promoted growth, enhanced physical indices, and reduced lipid deposition in muscle and hepatopancreas of juvenile S. prenanti. Quadratic regression analysis of WGR, SGR, PER, and FCR indicated that the optimal dietary bile acid supplementation level for juvenile S. prenanti ranges from 166.67 to 192.86 mg/kg.

References

[1] Wen AX, Zeng JK, He T. Analysis of nutritional components in muscle of Schizothorax prenanti[J]. Reservoir Fisheries, 2003, 23(1): 13-15.

[2] Wang JT, Song JY, Li HT, et al. Effects of emulsifiers on growth and blood biochemical indices of Jian carp[J]. Journal of Dalian Fisheries University, 2009, 24(3): 257-260.

[3] Liu ZY, Wang JP, Liu N. Effects of emulsifiers on intestinal microflora and immune function in broilers[J]. China Animal Husbandry & Veterinary Medicine, 2013, 40(8): 60-63.

[4] Reinhart GA, Mahan DC, Cera KR. Effect of group size and feeding regimen on nutrient digestibility studies with weanling pigs[J]. Journal of Animal Science, 1989, 67(10): 2684-2691.

[5] Pullen DL, Polin D. Effect of bile acids and diet composition on lipid absorption in chickens with cannulated bile ducts[J]. Poultry Science, 1984, 63(10):

2020-2026.

[6] Wang JT. Effects of dietary salt, DL-carnitine complex, and bile acids on growth, physiological function, and body color of channel catfish[D]. Master' s thesis. Suzhou: Soochow University, 2008.

[7] Wang H. Effects of different lipid sources and bile acids on growth performance and fatty acid composition of Macrobrachium rosenbergii[D]. Master' s thesis. Yangzhou: Yangzhou University, 2010.

[8] Zhou SY, Liu YJ, Liang HO, et al. Effects of dietary bile acids on growth and body composition of cobia (Rachycentron canadum)[J]. South China Fisheries Science, 2010, 6(4): 20-25.

[9] AOAC. Official methods of analysis of AOAC International[M]. 16th ed. Arlington, VA: Association of Analytical Communities, 1995: 1094.

[10] Chou BS, Shiau SY. Optimal dietary lipid level for growth of juvenile hybrid tilapia, Oreochromis niloticus × Oreochromis aureus[J]. Aquaculture, 1996, 143(2): 185-195.

[11] Hu TE, Wang L, Zhang CX, et al. Effects of dietary bile acids on growth performance, body composition, and nutrient apparent digestibility in bullfrogs (Rana catesbeiana)[J]. Acta Hydrobiologica Sinica, 2015, 39(4): 677-685.

[12] Deshimaru O, Kuroki K, Yone Y. Suitable levels of lipids and ursodesoxycholic acid in yellowtail[J]. Bulletin of the Japanese Society of Scientific Fisheries, 1982, 48(9): 1265-1270.

[13] Sun JZ, Wang JY, Ma JJ, et al. Effects of dietary lipid level and bile acid supplementation on growth, body composition, and lipid metabolism of juvenile turbot (Scophthalmus maximus)[J]. Oceanologia et Limnologia Sinica, 2014, 45(3): 617-625.

[14] Maita M, Tachiki H, Kaibara A, et al. Pharmacological effect of ursodeoxycholic acid in juvenile eel[J]. Nippon Suisan Gakkaishi, 1996, 62(1): 129-130.

[15] Xie ZG, Niu CJ. Effects of Kelikang on growth of rainbow trout[J]. Feed Research, 2002(10): 22-25.

[16] Lin SM, Ye YT, Luo L. Effects of bile acid additive on growth of gibel carp (Carassius auratus gibelio)[J]. Guangdong Feed, 2003, 12(3): 14-15.

[17] Tan YG, Wei WZ, Zeng DS. Effects of dietary bile acids on growth performance of gibel carp (Carassius auratus gibelio)[J]. Guangdong Feed, 2008, 17(1): 25-26.

[18] Liu JS, Yang YZ, Wang JR, et al. Research progress on nutritional functions and mechanisms of bile acids[J]. China Feed, 2010(6): 35-37, 43.

[19] Kim SK, Matsunari H, Takeuchi T, et al. Effect of different dietary taurine levels on the conjugated bile acid composition and growth performance of ju-

venile and fingerling Japanese flounder Paralichthys olivaceus[J]. Aquaculture, 2007, 273(4): 595-601.

[20] Xiang X, Zhou XH, Chen J, et al. Effects of lactic acid on growth and feed utilization of crucian carp[J]. China Feed, 2009(11): 40-41.

[21] Sun X, Yang GY. Current research status of bile acids' effects on glucose and lipid metabolism[J]. International Journal of Endocrinology and Metabolism, 2008, 28(5): 323-325.

[22] Huang BS, Li BS, Zhang LM, et al. Effects of bile acids on growth, lipid metabolic enzymes, and serum biochemistry of juvenile turbot (Scophthalmus maximus)[J]. Journal of Shanghai Ocean University, 2015, 24(5): 737-744.

[23] Xiang X, Zhou XH, Chen J, et al. Effects of dietary lipid level on growth performance, body composition, and serum biochemical indices of juvenile Onychostoma sima[J]. Chinese Journal of Animal Nutrition, 2013, 25(8): 1805-1816.

[24] Chatzifotis S, Panagiotidou M, Papaioannou N, et al. Effect of dietary lipid levels on growth, feed utilization, body composition, and serum metabolites of meagre (Argyrosomus regius) juveniles[J]. Aquaculture, 2010, 307(1/2): 65-70.

[25] Watanabe M, Houten SM, Mataki C, et al. Bile acids induce energy expenditure by promoting intracellular thyroid hormone activation[J]. Nature, 2006, 439(7075): 484-489.

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