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WE MAKE AQUACULTURE PROGRESS

ROMET® 30

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Romet® 30 is a feed grade antibacterial premix of sulfadimethoxine (SDM) and ormetoprim (OMP) developed for aquaculture. Romet® 30 contains 30% active ingredients (250 g/kg SDM and 50 g/kg OMP).

In 220 out of 242 (> 90%) commercial field trials, Romet® reduced mortality in US catfish by more than 20% in 24 hours. Romet® was fed at its standard dose of 50 mg active ingredient per kg body weight for 5 days (1).

The ormetoprim (OMP) in Romet® potentiates the sulfadimethoxine (SDM), reducing resistance potential and increasing efficacy.

Romet® a potentiated sulfonamide with quick action, minimal resistance and superior stability

Romet® can be added to feed prior to extrusion and pelleted without significant loss of activity. Trials show that 92 – 99 % of the initial Romet® potency was retained several months after feed processing. Romet® 30 has a two year shelf life in unopened bags while being stored under cool and dry conditions.

» Table 1

Stability of Romet® in pelleted fish feed (pelletizing temperature; 90˚C) (1).

Storage (temperature)	Storage (temperature)	Storage (months)	Average retention of Romet® (%)
˚F	˚C		
70	21	6	99
70	21	12	98
98,6	37	6	99

» Table 2

Stability of Romet® in extruded, floating fish feed (extrusion temperature; 130˚C) (1).

Storage (temperature)	Storage (temperature)	Storage (months)	Average retention of Romet® (%)
˚F	˚C	Initial after extrusion	95
113	45	3	96
98,6	37	6	92
70	21	6	96

Significant broad spectrum activity

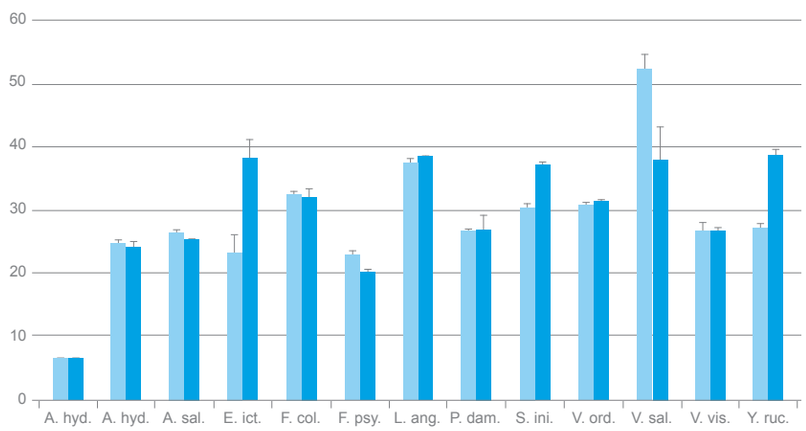
In the USA Romet® is approved for control of enteric septicemia caused by *Edwardsiella ictaluri* in catfish and furunculosis caused by *Aeromonas salmonicida* in salmon and trout.

Romet® is recognized as very effective against a wide variety of gram positive and gram negative bacteria, and is used in several countries for treatment of bacterial infections in aquatic animals caused by *Vibrio, Aeromonas, Edwardsiella* and *Staphylococcus* strains.

Disc sensitivity studies and minimum inhibitory concentration (MIC) studies done in the USA (figure 1 and 2) show that Romet® is active against a big variety of aquatic pathogens (2).

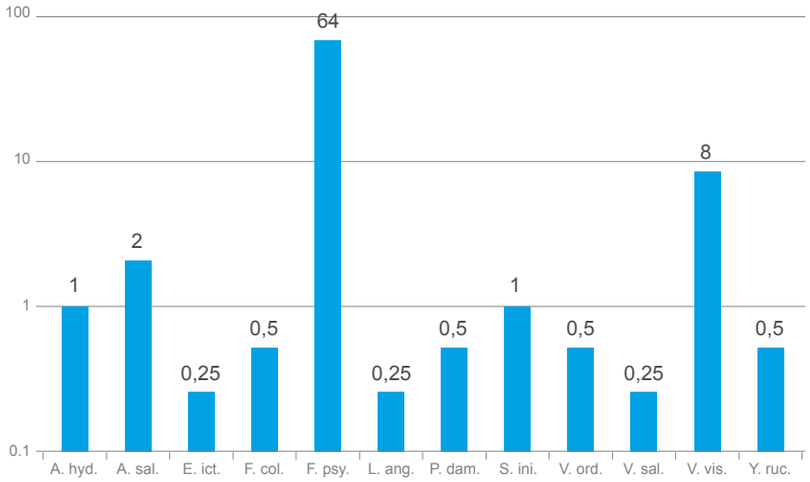
» Figure 1

Romet® Disc Sensitivity Diameters (mm) + SDEV to a Variety of Bacterial Fish Pathogens. Resistant (<10), Intermediate (11-15) or Susceptible (>16)].



» Figure 2

Minimum Inhibitory Concentration of Romet® (mg/L) for a Variety of Fish Pathogens Using the 96 Well Plates.



Sensitivity study from Thailand

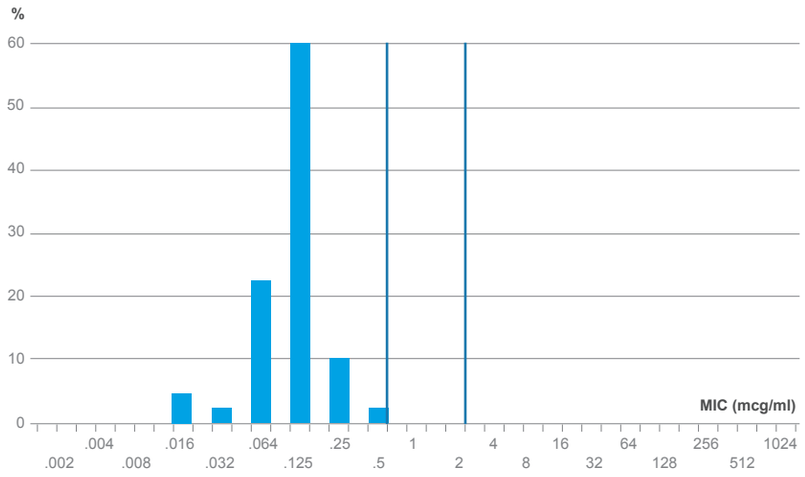
Four antimicrobial agents approved in Thailand (and the USA) for aquaculture use (amoxicillin, oxytetracycline, sulfadiazine/trimethoprim (SXT) and sulfadimethoxine/ormetoprim (Romet®)) were tested for their in vitro antimicrobial activity against clinical *Streptococcus* and *Vibrio* isolates.

Streptococcus strains were isolated from kidney of diseased tilapia (*Oreochromis niloticus*) (figure 3) and *Vibrio* strains were obtained from hepatopancreas of diseased black tiger shrimp (*Penaeus monodon*) or pacific white shrimp (*Litopeneaus vannamei*) (figure 4).

The study concluded that, with respect to MIC testing and possible implication of seawater effect, Romet® is a highly effective antimicrobial against *Streptococcus* in tilapia and *Vibrio* in penaeid shrimp (3).

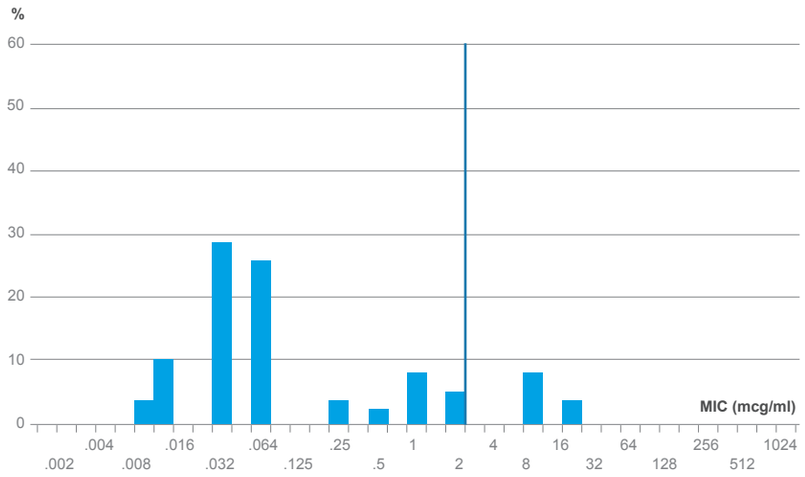
» Figure 3

Frequencies of minimum inhibitory concentrations (MICs) observed for Romet® against 50 *Streptococcus* isolates associated with disease in tilapia.



» Figure 4

Frequencies of minimum inhibitory concentration (MICs) observed for Romet® against 50 *Vibrio* isolates associated with disease in penaeid shrimp.



New patented application of Romet® for use as a parasiticide

Ciliate infestations in aquaculture and ornamental fish are global problems. Recent trials from Japan show that Romet® could be cost effective in controlling those infections caused by *Ichthyophthirius multifiliis* and *Cryptocaryon irritans.* PHARMAQ has licensed the rights to use Romet® for this application from the patent holder, Nippon Suisan Kaisha Ltd., (Nissui). The treatment regime as a parasiticide is 15 mg active ingredient per kg body weight per day for 14 days (4).

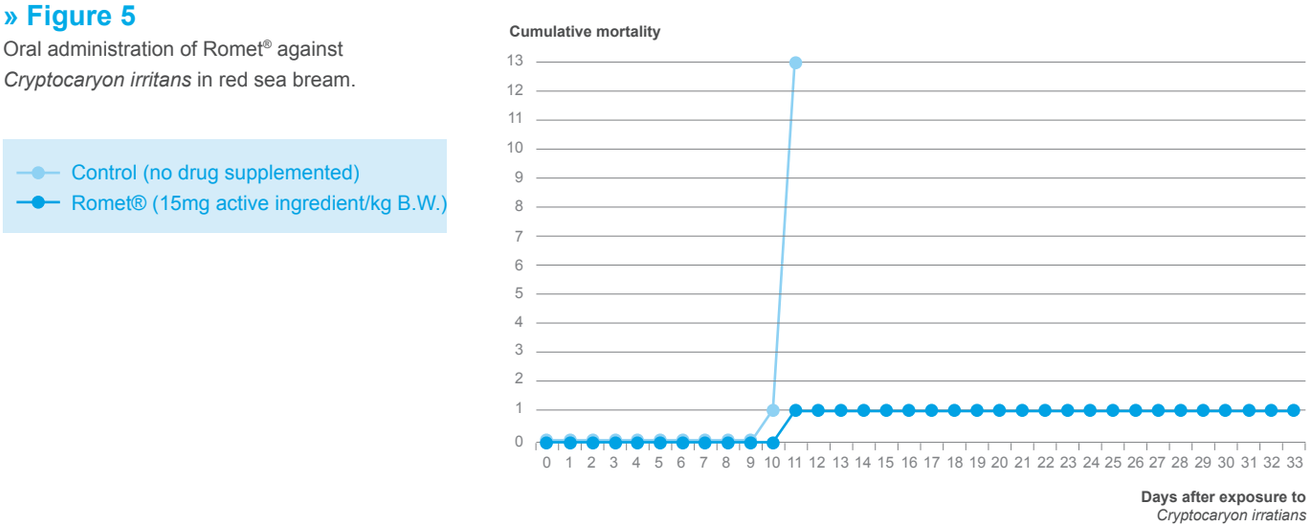
Red sea bream were exposed to *C. irritans* in an aquarium, divided into two groups and transferred to separate tanks.

One group was treated with Romet® for 14 days after exposure to *C. irritans* and a similar group was used as untreated control. In the control group, fish lost their appetite and their eyes became opaque due to heavy infection with *C. irritans* and, eventually, 100 % mortality was recorded. In the group treated with Romet®, there were no *C. irritans* signs observed on surviving fish at 33 days after the exposure and no mortality was observed except for one fish due to cannibalism (figure 5).

In the challenge trial with *I. multifiliis,* the results were similar to results shown with *C. irritans* (figure 6).

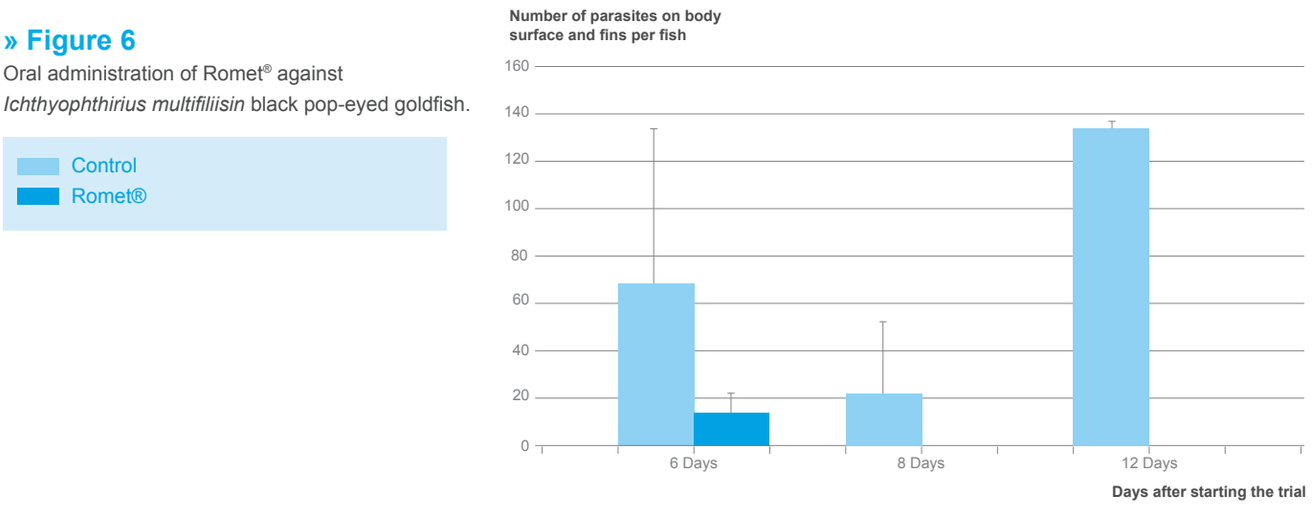
» Figure 5

Oral administration of Romet® against *Cryptocaryon irritans* in red sea bream.



» Figure 6

Oral administration of Romet® against *Ichthyophthirius multifiliisin* black pop-eyed goldfish.



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Safe and economical in use

Romet® does not cause any toxicity problems in fish and tissue examinations reveal no changes in muscle, kidney and other vital organ samples after treatment. Withdrawal time of Romet® varies per country of registration, normally from 5 – 40 days; and is typically dependent of water temperature (colder water leads to longer withdrawal time).

Compared to other drugs Romet® has a short depletion time in the body and is rapidly broken down in feces and aquatic sediments. The recommended dose is only 50 mg per kg body weight for 5 days, which is what makes Romet® a drug of choice for fish farmers around the world.

Mode of action

The potentiated sulfa drug Romet® interferes with folic acid production, an essential substance for cell wall synthesis of the bacteria. This takes place on two vital steps. Sulfadimethoxine (SDM) prevents the formation of dihydrofolic acid from para-aminobenzoic acid (PABA) and pteridine. Ormetoprim (OMP) interferes in the following step of transferring dihydrofolic acid into tetrahydrofolic acid, both important steps in the synthesis of bacterial cell walls. As a result, bacteria unable to successfully form cell walls will die allowing the host aquatic animal to overcome the disease infection.

How to use Romet®?

Romet® 30 is very versatile and user friendly. It can be applied into or onto the feed in a number of ways, including:

- Suspended in water (gelatin solution) and spread onto the feed. Do not use oils as oils tend to bring out the bitter taste of ormetoprim.
- Romet® is very heat stable. And can be mixed into the feed before pelletization or extrusion.
- Used as a top dressing Romet® can be sprinkled on top of feed before feeding.
- Bio-encapsulated in live feed such as artemia is also a novel possibility.

Recommended dosage

Establish the weight of the fish to be treated. Calculate the amount of feed needed to feed the fish per day according to fish size and water temperature (or recent actual feeding rates). 16.7 grams of Romet® 30 is needed per 100 kgs of fish weight per day (= 50 mg active ingredient per kg body weight eating 1kg feed per day), as described in Table 3 below. It is recommended to review local labels on the Romet® bags for correct use in your specific country.

For addition of Romet® to feed after pelletization or extrusion, prepare a slurry by suspending Romet®30 in a 5% gelatin solution. Gently coat the pelleted feed with the slurry and allow drying for several hours before storage. As a general rule, 1 liter of slurry is required to coat 25 kgs of pellets. Refer to dosage levels in Table 4 for recommended level of use.

» Table 3

Romet® for mixing into the feed 50mg / kg body weight for 5 days.

Daily feed intake (per cent of body weight)	Romet® 30 per metric ton feed (kg)	Biomass (fish, shrimp medicated per ton of feed 5 days treatment (kgs)
1	16,7	20 000
2	8,4	10 000
3	5,6	6 667
4	4,2	5 000
5	3,3	4 000
6	2,8	3 333

» Table 4

Romet® for coating of pellets (on the farm use).
1 liter slurry per 25 kgs feed (40 liter per ton).
50 mg / kg body weight for 5 days.

Daily feed intake (per cent of body weight)	Romet® 30 per liter slurry (grams)	Biomass (fish, shrimp) medicated per ton of feed 5 days treatment (kgs)
1	417	20 000
2	208	10 000
3	139	6 667
4	104	5 000
5	83	4 000
6	69	3 333

» Table 5

Romet® as a paracsticide for controlling ich and crypto. 15 mg per kg body weight for 14 days.

Daily feed intake (per cent of body weight)	Romet® 30 per metric ton feed (kg)	Biomass (fish, shrimp) medicated per ton of feed 14 days treatment
1	5,01	7 143
2	2,52	3 571
3	1,68	2 381
4	1,26	1 786
5	0,99	1 428
6	0,84	1 190

Romet® has a part to play in total protection strategies in aquaculture

PHARMAQ AS is one of the leading suppliers of effective and safe vaccines for the global aquaculture industry.

Used correctly, antibiotics can be useful tools in a total fish management program.

There are no miracle drugs available, and antibiotics should typically be used under veterinary supervision.

Other tools that should be included to the benefit of fish welfare and a sustainable aquaculture are safe and effective vaccines, immunostimulants, good husbandry practices, good management practices and focus on environmental issues such as e.g. water quality and water treatment programs.

» Please visit our web site www.pharmaq.com for further information about PHARMAQ and our products.

Romet® is distributed by:

Main references

1. Roche internal research data. (Roche was the first owner of Romet®).
2. Powell, D.B., Palm, R.C. (2001) Romet Sensitivity of Commercially Important Fish Pathogens, ProFishent.
3. Wongtavatchai, Janenuj. (2006) Minimum Inhibitory Concentrations of Antimicrobials against Vibrio spp. and Streptococcus spp. obtained from clinical isolates, Chulalongkorn University Bangkok.
4. Nissui patents: PCT/JP2008/069673 and PCT/JP/2010/57330 WO09/057653 (US2010-311759, EP2213169) and WO2010/125991