

[*Anti-Cancer Drugs*, 8, 482-488 (1997)]

[Lab. of Microbiology]

**Irreversible Cytotoxic Effect of a Novel Lowly Immunosuppressive Antitumor
Fluorouridine Derivative, UK-21.**

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To elucidate the molecular mechanisms of antitumor activity of 2',3',5'-tris-*O*-[*N*-(2-*n*-propyl-*n*-pentanoyl)glycyl]-5-fluorouridine (UK-21), the effect of the drug was examined on cell proliferation, cell cycle progression and macromolecular syntheses in comparison with 5-fluorouracil (5-FU), 5-fluorouridine (5-FUR) and 5-fluorodeoxyuridine (5-FUDR). Cytotoxic effects of UK-21 and 5-FUR on KB cells are irreversible, while those of 5-FU and 5-FUDR were reversible. UK-21, 5-FUR and 5-FU showed a linear relationship between exposure time and IC₅₀ in the colony formation assay, but 5-FUDR did not. UK-21 and 5-FUR, but not 5-FU and 5-FUDR inhibited the incorporation of [³H]-uridine, while UK-21 and 5-FUDR, but not 5-FUR and 5-FU inhibited the incorporation of [³H]-thymidine. In conclusion, UK-21 is a cell cycle non-specific inhibitor as well as 5-FUR and 5-FU in contrast to 5-FUDR. Irreversible cytotoxic effects of UK-21 like 5-FUR exert through inhibition of RNA synthesis.

[*Antonie van Leeuwenhoek*, 71, 207-215 (1997)]

[Lab. of Microbiology]

**Sexual Co-flocculation by Heterothallic Cells of the Fission Yeast
Schizosaccharomyces pombe modulated by Medium Constituents.**

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Novel simple synthetic media for inducing sexual co-flocculation in a short time after mixing heterothallic fission yeast (*Schizosaccharomyces pombe*) cells of h⁻ and h⁺ were devised; The most effective of these, mannose synthetic medium (MSM), contains 0.4% mannose as a carbon source in addition to galactose, KH₂PO₄ (pH4.0) and 4 vitamins. The addition of galactose to the medium suppressed the asexual self-flocculation but rather promoted the sexual co-flocculation. By transferring and mixing h⁻ and h⁺ cells grown in malt-extract broth plus galactose into MSM, these heterothallic strains were revealed to be sexually ready through a long period of the log to stationary phases. Furthermore, a variety of C sources and NH₄Cl at various concentrations in various media were examined for their effects upon sexual co-flocculation, conjugation and sporulation at 26°C and 30°C.

[*J. Gen. Appl. Microbiol.*, 43, 169-174 (1997)]

[Lab. of Microbiology]

**Induction of Sexual Co-flocculation of Heterothallic Fission Yeast
(*Schizosaccharomyces pombe*) Cells by Mating Pheromones.**

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Heterothallic fission yeast (*Schizosaccharomyces pombe*) cells preincubated with sex pheromone, P- or M-factor of the obverse mating-type cells, in MSM, results in remarkably increased sexual co-flocculation with obverse mating-type cells almost without time lag. By contrast, comparable flocculation requires over 1 h if untreated control cells are mixed with obverse mating-type cells. The agglutinin of P cells is more inducible than that of M cells. These pheromonal inductions of sexual co-flocculation are inhibited by the addition of cycloheximide or tunicamycin during preincubation but not by chloramphenicol or hydroxyurea. These results demonstrate that mating pheromones of fission yeast have another important role to induce sexual co-flocculation (agglutinability). Using our experimental system of preincubation with sexual pheromones, we show that M-agglutinin is heat-stable and its induction is inhibited by tunicamycin, but that P-agglutinin is heat-labile and its induction is only partially inhibited by tunicamycin.

[*Natural Medicines*, 50, 371-377 (1996)]

[Lab. of Herbal Garden]

**Studies on the Resources of "Kijitsu", the Immature Orange Fruits (1).
Possibility of New Origin for the Resource of "Kijitsu".**

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Use of immature fruits of the two new types of orange, from "Natsumikan," as a resource for "Kijitsu," dried immature orange fruits, was studied. The yields after drying of these two types orange fruits were about the same as those of "Natsumikan," "Kawano-natsudaidai," "Daidai," and "Hassaku." The total ash contents, and the amounts of extracts were also the same. Their naringin contents determined by HPLC, were not related to the harvest time, but to the size of the fruit. The naringin contents decreased as the size of fruits increased. The quality of "Kijitsu" prepared from these two new strains was shown to be the same as that of traditional ones from "Natsumikan" etc., when the size of fruits to be harvested was standardized.