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CHANGING DRUG SELLER BEHAVIOR ON CHILD DIARRHEA MANAGEMENT: EFFECTIVENESS OF TRAINING PROGRAM AND IMPLICATIONS OF KNOWLEDGE-PRACTICE GAP

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Lack of knowledge is often attributed to problematic practice by non-professional drug sellers. Most community pharmacies in Thailand are staffed by non-professionals who play dual roles of prescribing and dispensing. Training courses have been offered by government agencies attempting to improve quality of care by providing knowledge to drug sellers. This paper is part of a study to evaluate effects of multiple interventions on drug seller behavior. It aims to assess effects of training on knowledge and practice, and examine whether practice follows knowledge, using watery diarrhea in children under five as tracer condition.

A control-intervention and pre-post design was used. Eight districts in Bangkok were selected and matched into four pairs. Districts in each pair were randomly assigned as control and intervention districts. Seventy-eight community pharmacies were selected randomly from the districts. A training program, emphasizing case management for diarrhea in children, was offered to drugstore staffers in the intervention group. Knowledge was evaluated using open-ended questionnaire interviews. Dispensing practices were assessed by two simulated client surveys. The interviews and surveys were conducted twice—before and after training.

Pharmacies in both groups responded to the case with few questions and little advice. Dispensing of ORS only was found in 6.9 and 4.7% of the encounters before training for the control and intervention groups respectively. After the training, it was dispensed in 2.3% of the encounters in the control and 3.5% in the intervention group. Anti-diarrheal and anti-microbial drugs were dispensed in over 90% of the encounters, sometimes with ORS. Slight improvement in knowledge was seen in some aspects after training. However, while ORS-only was dispensed in fewer than 10% of encounters, around 20% of interviewees indicated they would dispense only ORS for such case. Despite slight improvement of knowledge on some aspects of case management after training, the program failed to improve practice. Better knowledge does not necessarily lead to better practice.

NOVEL POLYSACCHARIDE GEL FROM DURIAN FRUIT-HULLS: BIOLOGICAL EFFECTS IN ANTIBACTERIA AND HEALING WOUND

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A new water soluble polysaccharide gel (PG) isolated from dried fruit-hulls of durian was introduced. Sugars component in PG composed of arabinose, rhamnose, fructose, glucose and galacturonic acid. Biological effects of PG in antibacteria and healing wounds were investigated. In vitro antibacterial activity was performed to determine the susceptibility of microorganisms to PG. Seven strains of tested bacteria were susceptible to aqueous solution of PG according to agar diffusion susceptibility test. Sharp and clear inhibition zones were observed on medium of Mueller Hinton Agar with PG at concentration down to 0.32% against Staphylococcus epidermidis, Micrococcus luteus, Bacillus subtilis, Lactobacillus pentosus and Escherichia coli, at concentration 0.625% against Staphylococcus aureus and at 1.25% against Proteus vulgaris. Film formulation of PG composed of a plasticizer, 10% propylene glycol based on PG weight, was prepared by a casting/solvent evaporation method to obtain satisfactory film dressing. Preparation of PG film also showed bacterial inhibitory activity on agar plate. Effect of PG film dressing on healing wounds was performed in vivo in pig skin. Full thickness excisional wounds on skin of young pigs were treated by covering with PG film dressing compared with a conventional treatment (control) by applying 1% povidone iodine on wounds. Wound size was measured and changed a new dressing every 3 postoperative days. Film dressing of durian gel showed good wound healing effect. The result of wound closure demonstrated by the decreasing of wound area significantly (P<0.05) in treated group at day 12. The results suggest that new antibacterial film dressing of PG has benefit in pharmaceutical and medical applications.

**BACTERICIDAL EFFECT OF NEW POLYSACCHARIDE FROM FRUIT-HULLS OF DURIAN**

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Antimicrobial property of polysaccharide gel (PG) from fruit-hulls of durian (Durio zibethinus L.) was investigated to find a novel antimicrobial polysaccharide. In vitro activity was performed to evaluate the antibacterial activity of PG. The investigation found that PG showed inhibitory activity against 7 strains of tested bacteria. Broth microdilution method was used to determine a quantitative antimicrobial activity of PG. Minimal Inhibitory Concentration (MIC) of PG against M. luteus, S. epidermidis, B. subtilis, E. coli and P. vulgaris was 6.4 mg/ml and against S. aureus and L. pentosus were 12.8 and 25.6 mg/ml, respectively. Time-kill study demonstrated killing effect of PG against susceptible bacteria, the results showed that colony counts of bacteria were declined to zero with 25.6 mg/ml of PG at 12 hours against B. subtilis, at 16 hours against M. luteus, E. coli and P. vulgaris, at 20 hours against S. aureus and S. epidermidis. Whereas the colony count of L. pentosus was declined to zero with 51.2 mg/ml of PG at 8 hours. Examination of bacterial cells exposed to PG in normal saline solution under scanning electron microscope appeared an alteration on cell surface of bacteria. The mechanisms of action of PG against bacteria while not yet elucidated, it seems to relate to nature and sugar composition of PG.

**FILM FORMING PROPERTIES OF POLYSACCHARIDE GEL FROM DURIAN FRUIT-HULLS AND FILM-DRESSING PREPARATION**

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Polysaccharide gel (PG) was extracted from dried fruit-hulls of durian (Durio zibethinus L.). The PG product found to be useful for pharmaceutical preparations. Film-forming property of PG was investigated to evaluate its application as a film preparation in pharmaceuticals. Films of PG was prepared by a casting / solvent evaporation method from PG and mixture of aqueous solutions of PG with plasticizer using glycerin, propylene glycol, PEG 400 and PEG 6000, successively. Satisfactory film products were obtained. The mechanical properties of PG film was investigated by using Instron Universal Tester instrument. Films of PG polymer with plasticizers of 10% glycerin, 15% propylene glycol, 30% PEG 400 or 2% PEG 6000 based on weight of PG polymer were found to be most satisfactory which was enough slightly hard and tough indicated by high values of Young's modulus and % strain at break. Moisture sorption of PG films plasticized with PEG 400 was highest in comparison with PG films plasticized with PEG 6000, glycerin, propylene glycol and PG film without plasticizer. The chromatogram pattern of IR spectrum of plasticizers, PG film with plasticizer and PG film without plasticizer were compared, no new product was detected. Surface and cross section of PG film layer with and without plasticizer, film homogeneity of backing layer and adhesive layer were determined by SEM technique. A fine homogenized films was obtained. Adhesive properties was determined by peel adhesion test (180-degree angle). Ultimate tensile strength was 12.4 Newton. The results suggest that natural polymer of PG isolated from durian fruit-hulls has film forming properties that are useful for pharmaceutical preparations. A novel water soluble dressing of PG films was satisfactorily prepared. Good film product was obtained.

Acidic polysaccharide gel (PG) isolated from durian fruit-hulls has recently been introduced as a natural water soluble polymer. The polysaccharide composed of, repeating sugar unit of long or branch chain heteropolysaccharide, sugar component including arabinose, rhamnose, fructose, glucose and especially galacturonic acid was found to be a major component as similar to some other natural surfactant including gum. Aqueous solution of 4% polysaccharide gel (PG) showed apparent pH of 2.29±0.05 and 617.81±5.00 cPs viscosity. A rheological study of PG solution showed a non-Newtonian pseudoplastic behavior. Increasing PG concentration resulted in increasing viscosity. Effect of heat, pH, electrolytes, organic solvents and preservatives on PG viscosity was determined. The results indicated that PG has good potential in wide range of applications in pharmaceutical and cosmetic preparations. Formulations of vitamin E gel and lotion using PG as a surfactant were established. Satisfactory products of vitamin E gel and lotion were obtained. The results suggest that natural acidic polysaccharide from waste of durian fruit-hulls has benefit as a valuable material of commercial importance.
Polysaccharide gel (PG) was isolated from dried fruit-hulls of durian (*Durio zibethinus* L.). Film of PG was prepared by a casting/solvent evaporation method as a mucoadhesive film for treatment of sore mouth. The mechanical properties of PG films with plasticizers using a stress-strain tensile test were investigated. Tensile strength, strain or elongation, Young’s modulus and toughness were used to characterize desirable film. IR chromatography patterns of PG film with and without plasticizers and those including 0.1% w/w triamcinolone acetonide were identical, indicating no interaction between the drug and film base. The PG film-dressings formulated in this study were satisfactory.

**EFFECT OF DURIAN GEL FROM FRUIT-HULLS ON ENTRAPMENT OF FATTY ACIDS AND GLUCOSE**

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The purposes of this study were designed to determine the effects of polysaccharide gel (PG) from fruit-hulls of durian (*Durio zibethinus* L.) on entrapment of fatty acids; oleic acid, stearic acid; and glucose. The fatty acids and glucose entrapment in vitro were investigated by using semi-permeable membrane dialysis and gut sacs of dissected jejunum of rat. Dialysate samples were analyzed against respective standards for oleic acid, stearic acid and glucose by using HPLC system. A significant relationship were found between the decreasing of released fatty acids and glucose from dialysis bags and everted rat jejunum with respect to increasing concentration of PG. These results suggest that in vitro study by using semi-permeable membrane dialysis may be applied for preliminary evaluation of PG regarding fatty acids and glucose absorption and PG is capable of entrapment of fatty acids and glucose.

**APPLICATION OF POWDERED CELLULOSE FROM DURIAN FRUIT-HULLS FOR PREPARATION OF DIRECT COMPRESSION TABLETS**

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Powdered Cellulose (PC) derived from durian fruit-hulls, an agricultural waste material, was found to be an interesting product in pharmaceutical preparation. Such value-added product from plant waste are of benefit in utilizing agricultural product more efficiently. Pharmaceutical properties of PC according to the method of NF XVIII indicated that pharmaceutical properties of PC was comparable to the commercial cellulose (Elcema P100). Pharmaceutical application of PC was studied to evaluate its application as an excipient in tablet preparation. The tablets of PC were prepared by direct compression and weight, thickness, hardness, friability and disintegration times were evaluated. Tablets of PC using 1,500 lbs/inch2 of compression force showed satisfactory results of mean values of hardness (15.8±0.7 kp), friability (0.0%) and disintegration time (6.7 min) comparable to tablets prepared from commercial MCC using 1,000 lbs/inch2 compression force, whereas Elcema P100 gave unsatisfactory product. Tablet of lactose monohydrate were prepared using 2,000 lbs/inch2 compression force, satisfactory comparable results were obtained in tablet formulation using 75% PF or 75% MCC, whereas 75% Elcema P100 gave unsatisfactory result. PC isolated from agricultural waste of durian fruit-hulls is of good potential to be a valuable product that can be used as an excipient for the preparation of tablet according to this study.
HYPOGLYCEMIC EFFECT OF HAMM (KHAMIN-KHRUEA, Coscinium sp.) IN RATS

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Hamm used in the present investigation was identified to be Coscinium sp., family Menispermaceae. The hypoglycemic effect of crude water extract of hamm (khamm-khruea, Coscinium sp.) in normal and diabetic male Wistar rats was demonstrated. Crude water extract of hamm (HW) fed at doses 0.10, 0.25, 0.50, 0.75 or 1 g/kg body weight significantly decreased blood glucose concentration at 30 min after 1 g/kg body weight glucose feeding. Decreases were 10.40, 10.97, 10.80, 11.57 and 14.75 %, respectively; as compared to the control group. Feeding HW in non-fasted, diabetic rats at single doses of 0.10, 0.50 and 1 g/kg body weight significantly decreased blood glucose concentration at 2, 3 and 4 hr. Repeated doses of HW were given to diabetic male Wistar rats at 0.10, 0.50 and 1 g/kg body weight or insulin injection at 5 IU/kg body weight or control group given distilled water, once daily, for 14 days. HW significantly decreased blood glucose concentration at day 7 to 374.33, 363.83, 387.06, 373.73 mg/dl, respectively; compared to the control group, 414.51 mg/dl; and at day 14 to 400.83, 407.38, 417.75, 399.54 mg/dl, respectively; compared to the control group, 448.60 mg/dl. No difference in blood glucose concentration was observed in normal male Wistar rats fed repeated doses of HW at 1 g/kg body weight, once daily, for 14 days compared to the control given distilled water. Acute toxicity test in rats showed that LD50 of HW was greater than 20 g/kg body weight. HW was purified by silica gel column chromatography using ethyl acetate : iso-propanol : NH3 ( 7:2:1 ) as mobile phase. Four fractions were obtained.

FORMULATION OF KETOPROFEN LIQUID FILLED HARD GELATIN CAPSULES FOR RECTAL USE

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Ketoprofen liquid filled hard gelatin capsules for rectal application were developed. The liquid formulations of 100 mg ketoprofen to be filled into capsules were prepared using different combinations of three cosolvents i.e., polyethylene glycol 1500, propylene glycol, with Tween 60 or Tween 80 or dimethyl isosorbide (DMI). The capsules were coated using hydroxypropyl methylcellulose in order to enhance gliding effect during applying to the rectum. It was found that the dissolution of the drug were higher when the concentration of Tween 60, Tween 80 or DMI were increased from 10% to 30%. Drug release of the formulation with 20% Tween 80 was faster than the formulation containing 20% DMI. In vivo evaluation of the selected ketoprofen rectal capsules using rabbits as the subject was also investigated and the data will be reported elsewhere.

POLYMER MATRICES OF HYDROXYPROPYL METHYLCHELULLOSE AND XANTHAN GUM FOR ORAL CONTROLLED DELIVERY OF DILTIAZEM HYDROCHLORIDE

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Matrices composed of hydroxypropyl methylcellulose (HPMC) and xanthan gum (XG) in the mixing ratio of 1:1 for controlled release delivery of diltiazem hydrochloride were investigated. The mixture of XG and HPMC was found to give higher retarding effect than only HPMC containing matrices. The matrices comprising this mixed polymers with the water-soluble filler (lactose) exhibited higher drug release than those containing water-insoluble filler (dibasic calcium phosphate). The matrices formulated using 3.5% mixed polymer and dibasic calcium phosphate or 7.5% mixed polymer and lactose gave their release profiles comparable to the commercial product (Cardil®, 120 mg diltiazem hydrochloride sustained release product). In vivo evaluations of these two developed formula were also carried out using rabbits as the subjects and the results will be reported elsewhere.