# Release Profile of $^{14}$C-Butachlor from Controlled Release Formulation Prepared with Alginate-Kaoline Matrix

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# Alginate와 Kaoline을 利用한 放出調節劑의 $^{14}$C-Butachlor 溶出特性

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## ABSTRACT

The herbicide $^{14}$C-butachlot[N-(butoxymethyl)-2-chloro-2', 6'-diethylacetanilide] labelled uniformly in benzene ring was incorporated in alginate-based granules to get controlled release properties. The influence of kaoline addition on the formulation characteristics and release profiles were evaluated under a closed dark and an opened sunlight condition. Incorporation efficiency of $^{14}$C-butachlor in alginate-kaoline matrices was over 91.8%. Formulation yield was decreased with increase of kaoline concentration. The release rate from all the granules prepared with alginate was slower than that from the commercial granule impregnated in zeolite. The release rate from the granule containing kaoline was dicreased as the kaoline content was increased under both conditions. Losses of butachlor from the leacheate solution of the alginate-kaoline matrices under an opened sunlight condition was diminished by increasing the kaoline content.

Key words : Controlled release formulation, Alginate-kaoline matrix, Release profile

## INRODUCTION

In modern agricultural practices, pesticide has become an indispensible essential to decrease crop losses by insect pests, diseases and weeds, and to upheave the crop productivity as well as quality. Increased input of pesticides in the crop environment has however led to concentration of social concern due to their biological activity. These adverse impacts are originated from the fact that the major portion of pesticides applied in practice enters to the environments without contributing to the control of the target organisms(10).

Formulation technology of controlled release has proven to be the most adequate conunter-measure to solve the side effects of pesticides. The technology imparts various advantages to active agents : reduction of acute toxicity and phytotoxicity, extension of activity, protection from environmental degradation, control of release pattern, masking of noxious materials, etc.(13). Various dispensers links synthetic polymers(1, 11, 14, 16, 18), natural polymers(9), inorganics(6) have been utilized as controlled release devices. Controlled release formulations prepared by using biopolymers such as starch(17, 19, 20, 21), lignin (22, 23), and algin(2, 3) are of special interest, because of the possible biological degradation of the matrices when the duration of action has

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finished, and the relatively low costs of some of the raw materials.

In particular, algin is a linear polysaccharide derived from browm seeweed. Sodium alginate, the common algin, is water soluble with thickening, suspending, emulsifying, stabilizing, water holding and gel forming properties. Alginate gel has been used as matrices for the controlled release of pesticides(7, 8, 15). A sustained release of microbial spores and cells from biopesticides incorporated in alginate granules has also reported by many workers(4, 5, 12) Diluted aqueous solution of sodium alginate is gelled to comparable tough gel beads by reaction with $Ca^{2+}$ or $Ba^{2+}$ ions, thus the incorporated active agents can be controlled the release profiles in the crop environments.

In order to investigate the development feasibility of controlled release formulation of butachlor using alginate, the granules formulated with different ratio of sodium alginate as gellant and kaoline as filler were prepared. The formulation properties and release profiles of the active ingredient from alginate-kaoline matrices in water under a closed dark and an opened sunlight condition was compared with commercial granule.

## MATERIALS AND METHODS

The present study was undertaken at Seibersdorf Laboratory of International Atomic Energy Agency, Seibersdorf, Austria.

### Chemicals

Radiolabelled butachlor[N-(butoxymethyl)-2-chloro-2', 6'diethyl-acetanilide] was obtained from Dupont(Lot No. 2512-243), which is uniformly $^{14}C$-labelled in benzene ring with 99% of purity. Radioactivity of the chemical was 24.9 mCi/mM. Cold butachlor technical was acquired from Monsanto with 94% of purity. Sodium alginate as gellant was reagent-grade from Fluka AG. Kaoline as filler was industrial-grade passed through 325 mesh sieve. The other chemicals for formulation, release study, and instrumental analysis were reagent or HPLC-grade.

### Formulation of Butachlor with Calcium Alginate Gel

Controlled release granules of butachlor by using various combinations of alginate and kaoline as a matrix were prepared as shown in Table 1 of formulation repices.

Sodium alginate equivalent to each formulation was dissolved in distilled water and then kaoline was added to the alginate solution while stirring with magnetic stirrer. The acetone solution of cold butachlor technical was dropwise added to the mixture and toluene solution of $^{14}C$-butachlor was finally dropped to the mixture at the level of $130\mu Ci (288 \times 10^6$ dpm) while stirring.

By use of the appratus modified from Connick (7), which is useful for small-scale processing assembled from laboratory glassware(Fig.1), the mixture slurry was added dropwise to a 300ml gellant bottle of 0.25M $CaCl_2$. The alginate beads substituted $Na^+$ with $Ca^{2+}$ was collected by

**Table 1**. Formulation recipes of $^{14}C$-butachlor* controlled release formulations using alginate and kaoline as matrix

| Component | Percent of weight | | | | |
|---|---|---|---|---|---|
| | BF1 | BF2 | BF3 | BF4 | BC* |
| Technical*** | 10 | 10 | 10 | 8.7 | 7 |
| Sodium alginate | 90 | 40 | 20 | 4.3 | - |
| Kaoline | - | 50 | 70 | 87 | - |
| Zeolite | - | - | - | - | 93 |

* Spiked level of $^{14}C$-butachlor was $130.3\mu ci (288.65 \times 10^6$dpms) per each formulation

** BC designated commercial granule prepared by impregnation process

*** Active ingredient content of technical was 94%

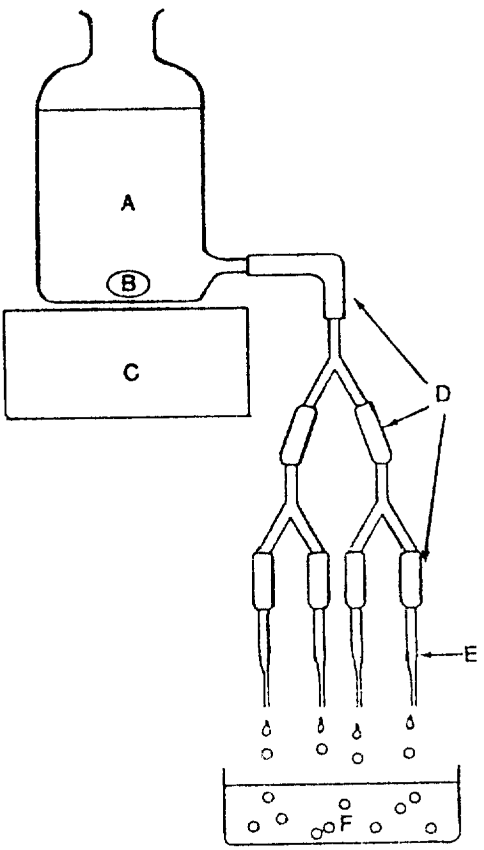

**Fig. 1.** Apparatus used to prepare controlled release formulation with alginate-kaoline matrix. A : 250ml of aspirator bottle, B : Stir bar, C : Magnetic stirrer, D : Rubber tubing, E : Disposable pipets, F : Dish containing gellant solution.

filtration through Büchner funnel. The bath, bottle, tubings, and beads were washed with about 400ml of distilled water. The filtrate and washings were combined and stored for the radioactivity count. Formulated granules were placed in petri dishes at room temperature to air-dry for 5 days and desssicated in vacuum dessicator for 4 days.

Reference granular formulation of butachlor was prepared by dissolving 1.5gm of cold butachlor technical and 112.8$\mu$Ci of $^{14}$C-butchlor in 100ml of acetone, adding 18.5gm of granular zeolite, mixing the slurry, and evaporation the acetone under rotary evaporator at 40℃.

### Release Profile of $^{14}$C-Butachlor in Water

For the experiment under a closed dark condition, the granules (58.1 to 75.4mg) were added to 750ml of a reconstituted fresh water (RFW) in 1L of aluminium foil-wrapped erlenmyer screw cap flask. RFW was prepared by dissolving 192mg of $NaHCO_3$, 120mg of $CaSO_4.2H_2O$, 120mg of $MgSO_4$ and 8mg of KCl to 1L of deionized water.

For the experiment under an openeed sunlinght condition, the granules (58.0 to 75.5mg) were placed into 750ml of RFW in glass dish of 185mm diameter and 85mm height.

All the vessels were placed under opened air, where the bottom was covered with white polyethylene sheet and the cover was installed with transparent acryl plate over 5cm above the vessels to prevent rainfall. Weight and temperature of the RFWs in the vessels were periodically checked to maintain the inital volume and to check the temperature of water.

All the tested samples were run in triple. Aliquots of 1ml were removed for determination of disssolved $^{14}$C-butaschlor with a Valco Digit Micropipetter, after which same portions of fresh RFW were added to the vessels. Release experiment was terminated after 25 day of release. A total of 1488ml of RFW was evaprated from the each dish under an opened sunlight condition. The cummulative temperature of RFW under an opened sunlight was higher than that a closed dark condition. After termination of the release study, all the granules were collected from each vessel to count the residual radioactibity in the granules.

### Analytical Procedure

Radioactivity of leacheate was counted by Beckman 9800 Liquid Scintillation Counter after the leacheate was mixed with 14ml of Aquasol cocktail (New England Nuclear Co., U.S.A.). Total radioactivity in the granules before and after release study was done by oxidizing the sample in Harvey Sample Oxidizer. Flow of nitrogen and oxygen was adjusted 100ml/min, and combustion time was 4 min Absorbent solution for the sample combustion was 10ml of 12.5% ethanolamine in methanol and cocktail was 10ml of PPO/POPOP in toluene. Percent recoveries of the combusted sample were 97% to 100% with an excellent linearity upto $0.75 \times 10^6$ dpms.

Thin layer chromatography was done by Kieselgel 60 F254 (5×20cm) in a solvent system of toluene+methanol+acetonitrile (50+50+1, vol%) and ethyl acetate+ethanol+acetic acid (50+50+1, vol%) to identify the degradation by-products during release study of the granules. Radioscanning of the TLC plates was performed by Dunnschicht Scanner II with scan range of 3000cpm at 10 sec of time constant and 120mm/hr of scan speed.

## RESULTS AND DISCUSSION

### Formulation Characteristics

Granules containing $^{14}$C-butachlor with sodium alginate were prepared by using calcium ions from their chloride salt as gelling agent in order to investigate gellant-related release differences under a closed dark and an opened sunlight condition. The granules formulated by the gell process resulted in uniform incorporation of the butachlor throughout the alginate matrix. Production yield was diminished by increasing the ratio of kaoline, which was caused by less amount of substitutive sodium ions by calcium ions in the alginate as shown in Table 2.

The increase of kaoline content in the alginate led to larger and heavier granules that were more spherical with less aggregation during dry process. In addition, the increased addition of kaoline, an inexpensive filler, efficiently reduced the amount of the more expensive alginate in the final products. BF1, which was formulated without kaoline, contained an estimated 61.1% alginate ; whereas BF4, which was prepared with 87% kaoline in the formulation process, contained about 3.6% alginate.

Incorporated amount of $^{14}$C-butachlor into alginate granules analyzed by sample oxidizer was compared with the amounts subtracted the activity of filtrate during the gelling process from the added activity as shown in Table 3. In general, the incorporated activity into the granules was increased by decreasing the amount of alginate. The incorporated rate was directly related to the activity in the filtrate. Since the formulation process involved dissolution of sodium alginate in water, the granules contained high portion of alginate required during the formulation process led to increase the dissolved activity in the filtrate. Theoritically calculated incorporation rate of the activity into the granule was always higher than the directly analyzed rates by sample oxidizer. These differences are probably resulted from the activity losses during dry process. However, as a general, the incorporated rate of the chemical into the alginate granules could be estimated by deducting the activity in the filtrate from the spiked amount.

**Table 2.** Product yield and characteristics of controlled release formulations prepared with different ratio of alginate and kaoline as matrix

| Formulation | Formulation Wt. processed(gm) | Product | | | |
|---|---|---|---|---|---|
| | | Dry Wt. (gm) | Alginate (%) | Kaoline (%) | Average Wt. of granule (mg) |
| BF1 | 10 | 14.6 | 61.6 | 0 | 0.94±0.01* |
| BF2 | 10 | 12.3 | 32.5 | 40.7 | 1.08±0.01 |
| BF3 | 10 | 11.2 | 17.9 | 62.5 | 1.57±0.03 |
| BF4 | 10 | 11.9 | 3.6 | 73.1 | 3.38±0.35 |
| BC | 20 | 19.8 | - | - | 0.96±0.18 |

* Standard deviations

**Table 3**. Incorporation efficiencies of $^{14}$C-butachlor into the granules formulated with different ratio of alginate and kaoline as matrix

| Formulation | Formulation efficiency of $^{14}$C-butachlor* by | | | | |
|---|---|---|---|---|---|
| | Theoretical | | | Analytical | |
| | Filtrate (× $10^6$ dpm) | Incorporated (×$10^6$ dpm) | Efficiency (%) | Incorporated (×$10^6$ dpm) | Efficiency (%) |
| BF1 | 21.07 | 267.61 | 92.7 | 265.01 | 91.8 |
| BF2 | 12.83 | 275.85 | 95.6 | 270.78 | 93.8 |
| BF3 | 10.68 | 277.99 | 96.3 | 275.40 | 95.4 |
| BF4 | 5.74 | 282.34 | 98.0 | 279.73 | 96.7 |
| BC | 9.27 | 279.41 | 96.8 | 273.09 | 94.6 |

* Spiked level of $^{14}$C-butachlor was 130.3uCi (288.675×$10^6$ dpms) per each formulation

**Release Profile of $^{14}$C-Butachlor in Water**

Butachlor release profiles from the granules which were obtained with alginate-kaoline matrices and the commercial product placed in FRW under a closed dark and an opened sunlight condition are illustrated in Fig. 2.

The commercial butachlor granule which was impregnated in/on granular zeolite released over 56% of the inputted activity within 4 days of release under the both conditions. Thereafter, the release pattern of the commercial granule under a closed dark followed $\sqrt{t}$ order, which was illustrated that a larger amount of the butachlor was released initially, and substantially smaller and decreasing amounts were released during the later stage of the life of the granules. The release profile of the commerical granule exhibited that approximately 50% of the active ingredient in the granule was deposited on the outer layer of the zeolite granule, which was easily discharged into the water. The rest 50% of the active ingredient was incorporated into the granule which showed a controlled release pattern more or less.

On the other hand, all the granules formulated with alginate-kaoline matrices resulted in controlled release profiles under a closed dark condition. BF1 formulated without kaoline released 76.35% of the total activity during 25 days of release, which was almost equivalent to the rate of the commercial granule. The release rate of the total activity from the granule was diminished with increase of kaoline content in the

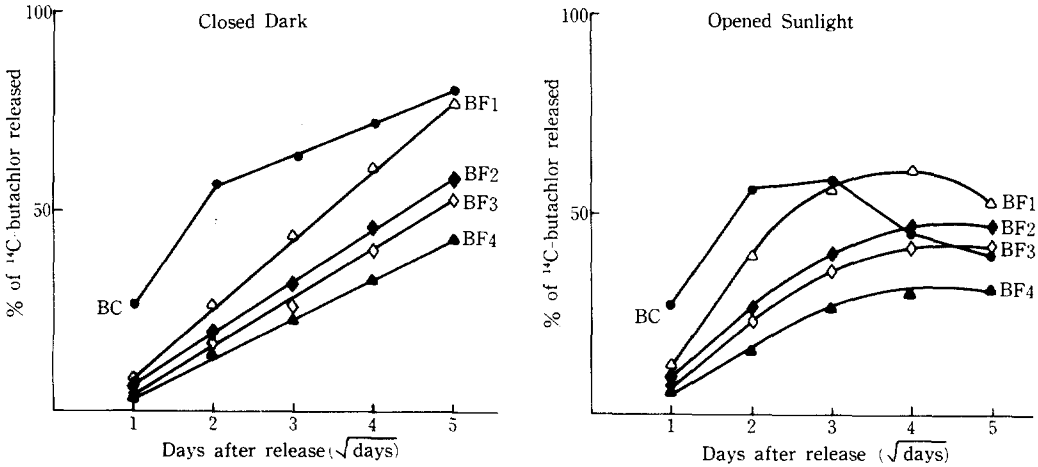

**Fig. 2**. Release profiles of $^{14}$C-butachlor from the granules formulated with different ratio of alginate and kaoline as matrix into reconstituted fresh water under a closed dark and an opened sunlight condition

matirx. BF4 formulated with 73.1% kaoline in the matrix released 43.27% of the total activity during 25 days of immersion.

Dissolved radioactivity of $^{14}$C-butachlor from the granules into RFW under an opened sunlight condition was quite different from those profiles under a closed dark condition. The commercial granule released 56.04% of the total radioactivity within 4 days of immersion, however, thereafter the dissolved activity in RFW was sharply decreased after 9 days of immersion, which might be caused by codistillation of the released activity with water evaporation during the release study. Likewise, dissolved profiles of the activity from the granules formulated with alginate-kaoline matrices into RFW gave different "$\sqrt{t}$ order" pattern, due to the codistillation effect of the released activity. Dissolved activity from BF1 granules in RFW was increased to 61.07% within 16 days of release, while the activity was down to 52.60% of total inputted activity after 25 days of release. This profile represented that the release rate of the activity from the granule was overcome the codistillation rate from the RFW within 14 days of release. Dissolved activity from other alginate-kaoline matrices(BF2 to BF4) in RFW was consistently increased until the end of release study.

**Distribution of $^{14}$C-Butachlor after Release Study**

Radioactivity distribution of the tested granules after 25 days of release study under a closed dark and an opened sunlight condition was summarized in Table 4, by analyzing the activity dissolved in the RFW and retained in the granules

Under a closed dark condition, over 95% of the total radioactivity was recovered with 2.4% to 5.14% of loss which were within the standard deviation ranges. Released rate of the activity from BF1 formulation was almost equal to the rate from the commercial granule during 25 days of release study. However, the rates from the granules formulated with alginate-kaoline matrices were diminished with increase of kaoline content.

Retained radioactivity in the granules after release study under an opened sunlight condition was consistently lower than that under a closed dark condition regardless of formulations. It is suggested that higher cummulative temperature of RFW during release study under former condition might accelerate the release rate of active ingredient from the granules. The radioactivity losses during release study under an opened sunlight condition were relatively quite high ranged from 24.56% to 44.79% of the initial activity. In order to clarify the nature of the losses, a concentrated portion of the leacheate solution was chromatographyed by TLC, compared with parent butachlor spot, and scanned by radioscanner. A similar procedure was also conducted to confirm the radioactivity retained in the granules after the release study. No spots on

**Table 4**. Distribution of $^{14}$C-butachlor of the granules formulated with different ratio of alginate and kaoline as matrix after 25 day of release study under a closed dark and an opened sunlight condition

| Formulation | Percent distribution of $^{14}$C-butachlor under | | | | | |
|---|---|---|---|---|---|---|
| | Closed dark | | | Opened sunlight | | |
| | Dissolved in RFW* | Retained in granule | Loss | Dissolved in RFW | Retained in granule | Loss |
| BF1 | 76.95±2.43** | 19.76±1.28 | 3.29 | 53.47±1.84 | 2.27±0.38 | 43.77 |
| BF2 | 58.34±3.88 | 39.26±2.89 | 2.40 | 47.72±1.55 | 15.50±1.83 | 36.78 |
| BF3 | 53.57±2.95 | 41.91±4.20 | 4.52 | 42.58±0.87 | 27.01±3.09 | 30.41 |
| BF4 | 43.60±2.45 | 51.58±3.63 | 4.82 | 31.30±1.12 | 44.14±2.23 | 24.56 |
| BC | 77.09±8.13 | 17.77±4.96 | 5.14 | 40.92±5.00 | 14.29±3.26 | 44.79 |

* RFW designated reconstituted fresh water

** Standard deviations

A total of 1,488 ml of water was evaporated during the release study

TLC plates and no responses by the scanner except the parent chemical molecule were detected, which meant that photodegradation of the parent compound was not taken place during the release study. In consequent, the losses of the released activity was resulted from the codistillation of the parent compound with water.

Retained radioactivity in BF1 formulation was much less than that in the commercial granule ; neverthless, the loss of the activity from the former was almost same as that from the latter. Dissolved radioactivity from BF1 in RFW was still higher than that of the commercial granule. Retained radioactivity in the granule was increased as the kaoline content in the granule was increased. The residual activity in RFW and the losses of the activity during release study were on the contrary decreased with increase of kaoline content.

Bioassay experiment of the granules in paddy field is required to elucidate the relations between optimum ratio of alginate-kaoline combination and the residual weed control effects.

In particular, emphasis on efficacy of the granules against weed seeds flowed into the paddy field with irrigation water has to be clarified in the future.

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## 摘 要

Alginate와 Kaoline을 貯臟媒體로 使用하여 製劑한 Butachlor[N-(butoxymethyl)-2-chloro-2′,6′-diethylacetamlide] 放出調節劑의 特性 및 主成分 溶出樣相을 暗條件과 日光露出 條件下에서 zeolite 吸着型粒劑와 比較試驗하였다.

Calcium alginate-Kaoline 貯臟體에의 butachior製劑率은 91.8%以上이었고 製品의 收率은 kaoline의 添加量이 增加할수록 減少하였다.

放出調節劑의 水中 主成分 溶出速度는 試驗條件에 關係없이 zeolite吸着型粒劑보다 緩慢하였고 kaoline의 含量이 增加할수록 그 速度는 顯著하게 減少하였다.

日光露出條件에서 水蒸氣와의 共蒸溜에 依한 溶出主成分의 減少率은 kaoline의 含量이 增加할수록 低下되는 傾向을 보였다.

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