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# Genotoxicity of Capsaicin in Cultured Human Lymphocytes

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*ABSTRACT* : **The clastogenic activity of capsaicin, a major pungent and irritating constituent of hot chili pepper, was evaluated in cultured human lymphocytes. Capsaicin (125, 250, and 500 μM) caused cytogenetic damage as determined by increased frequency of chromosome/chromatid aberrations compared to the solvent control. The mitotic indices were also decreased in a concentration-related manner in capsaicin-treated cells. Moreover, capsaicin suppressed [$^3$H]thymidine incorporation into lymphocytes. The clastogenicity and cytotoxicity of capsaicin towards human lymphocytes were evident without an external metabolic activation system. Taken together, these findings suggest that capsaicin is a genotoxic agent and may thus represent a potential health hazard in humans.**

**Keywords : capsaicin; chromosome aberration; human lymphocytes; clastogenicity**

## INTRODUCTION

Epidemiological and laboratory studies have shown that the majority of human cancers are attributable to environmental factors. Recently, attention has focused on carcinogens in food as potential causative factors of human cancer (Ames, 1983; Miller and Miller, 1986). Various spices have been used as appetizers, food preservatives, and traditional medicines. Hot green or red pepper (*Capsicum*) is one of the most widely used spices throughout the world (Govindarajan and Sathyanarayana, 1991). The principal pungent and irritating constituent of *Capsicum* fruits is capsaicin (*trans*-8-methyl-N-vanillyl-6-nonenamide; chemical structure shown in Fig. 1). The capsaicin content of hot red pepper ranges from 0.1 to 1.0% (Govindarajan and Sathyanarayana, 1991). It has been suspected that spicy foods may play a role in the etiology of human hepatic and gastrointestinal carcinogenesis. Capsaicin and chili extracts have been tested for mutagenicity in bacteria (Toth *et al.*, 1984; Nagabhushan and Bhide, 1985 and 1986; Gannett *et al.*, 1988; Vinitketkumnuen *et al.*, 1991; Azian and Blevins, 1995) and cultured mammalian cells (Nagabhushan and Bhide, 1985; Lawson and Gannett, 1989) with or without S9 activation, but results are discordant (see Table 1; recently reviewed by Surh and Lee, 1995). Capsaicin has been also reported to be clastogenic in rodents, inducing significant increases in the formation of micronuclei in mouse bone marrow (Villasenor and de Ocampo, 1994). The compound also inhibited DNA synthesis in the testes of Swiss mice (Nagabhushan and Bhide, 1985). Rats fed diets containing 10% chili pepper developed hepatomas (Hoch-Ligeti, 1951). In another study, dietary administration of capsaicin produced duodenal tumors in Swiss albino mice (Toth

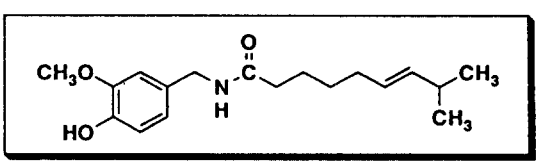


**Fig. 1.** Chemical structure of capsaicin.

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**Table 1.** Mutagenicity of capsaicin in bacterial and mammalian cells in culture

| Tester strain(s)/cell type | Hepatic S9 | Mutagenicity | References |
|---|---|---|---|
| *S. typhimurium* TA98, TA100, TA1535 | Aroclor 1254-induced rat | + | Nagabhushan and Bhide, 1985 |
| *S. typhimurium* TA98 | Aroclor 1254-induced rat | + | Nagabhushan and Bhide, 1986 |
| *S. typhimurium* TA98 | Aroclor 1254-induced rat | + | Toth *et al.*, 1984 |
| *S. typhimurium* TA98, TA1535 | Aroclor 1254-induced rat | − | Gannett *et al.*, 1988 |
| *S. typhimurium* TA98, TA100, TA1535 | Phenobarbital-induced rat | − | Buchanan *et al.*, 1981 |
| *S. typhimurium* TA98, TA100, TA1535 | - /+ (Source not specified) | − | Vinitketkumnuen *et al.*, 1991 |
| *S. typhimurium* TA100 | Source not specified | + | Azian and Blevins, 1995 |
| Chinese hamster V79 | Aroclor 1254-induced rat | − | Nagabhushan and Bhide, 1985 |
| Chinese hamster V79 | Syrian golden hamster* | + | Lawson and Gannett, 1989 |

*Hepatocytes used

*et al.*, 1984). Results from studies by other investigators suggest that capsaicin may act as a co-carcinogen or a tumor promoter (Agrawal *et al.*, 1986; Jang and Kim, 1988). A case-control study conducted in Mexico City (Lopez-Carrillo *et al.*, 1994) found that chili pepper consumers were at higher risk for gastric cancer than nonconsumers. However, it remains unclear whether capsaicin in hot chili pepper is a major causative factor in the etiology of gastric cancer in humans. Moreover, there are no reports of genotoxic effects of capsaicin in human cells. Considering the frequent consumption of capsaicin as a food additive and its current therapeutic application to management of patients with neuropathic diseases, not only the correct information on mutagenic and/or carcinogenic potential of this compound, but also understanding of the mechanism of its adverse actions is important. Here we report the clastogenic activity of capsaicin in cultured human lymphocytes. This is the first experimental investigation of capsaicin-induced genotoxicity in human cells.

## MATERIALS AND METHODS

### Chemicals

Capsaicin (purity, 98%), mitomycin C, cyclophosphamide, colcemid, dimethyl sulfoxide (DMSO), $NADP^+$, and glucose-6-phosphate were purchased from Sigma Chemical Co. (St. Louis, MO). All other solvents and chemicals used were commercial products of analytical grade.

### *In vitro* human lymphocyte assays

Human peripheral blood from young healthy female donors was cultured as described previously (Evans and O'Riordan, 1975). For each culture, 0.5 ml of heparinized whole blood was added to 5 ml of prewarmed KaryoMAX Peripheral Blood Cell Karyotyping Medium containing phytohemagglutinin and inactivated fetal calf serum (Gibco BRL, Gaithersburg, MD). Cultures were incubated for 48 h in a humidified 5% $CO_2$ atmosphere at 37°C before treatment with capsaicin. In experiments with S9 metabolic activation, cells were centrifuged at 1,000 rpm for 8 min after 48 h culture, and resuspended in the same medium plus S9 mix (S9 mix: medium, 1:4, v/v; prepared immediately before use) containing each test compound. Hepatic postmitochondrial supernatant used for S9 mix was prepared from Aroclor 1254-pretreated (500 mg/kg, i.p. for 5 consecutive days) male Sprague-Dawley rats weighing ~200 gram. S9 mix consisted of 10% S9 and NADP (4 mM) plus glucose-6-phosphate (5 mM). After 2 h capsaicin treatment, cells were washed twice with phosphate-buffered saline (pH 7.4), resuspended in media, and incubated for 22 h. Without S9 activation, cultures were treated for 24 h. The final DMSO concentration was <1%. Cyclophosphamide and mitomycin C were included as positive controls for treatment with and without S9 activation, respectively. Two hours before harvesting, colcemid (final concentration, 0.1 μg/ml) was added to each culture for mitotic arrest. Cells were collected by centrifugation and resuspended in 6 ml of prewarmed (37°C) 0.075 M KCl for 8 min at 37°C. Cells were pelleted then fixed in acetic acid-methanol (1:3, v/v). Coded slides were stained with Giemsa. For evaluation of clastogenicity, a total of 200 well-spread metaphase cells from each duplicate culture were scored for gaps, breaks, and exchanges. Only cells with 46 chromosomes were examined. We regarded an unstained region less tham the

width of a chromatid as gap and greater than the width of a chromatid as a break. Gaps were not included in the determination of the total frequencies of aberrant cells. The mitotic index was estimated from 2,000 cells per culture and expressed as percentages of control values (Sbrana *et al.*, 1984).

### Determination of [$^3$H]thymidine incorporation

The assay for thymidine incorporation was conducted by treating lymphocyte cultures with capsaicin in medium containing [$^3$H] thymidine (New England Nuclear Co., Boston, MA; 2-3 μCi/ml) for 24 hrs. After treatment, cells were pelleted then rinsed with phosphate-buffered saline (pH 7.4) containing nonradioactive thymidine (1.25 mM). Cell pellets were solubilized and the radioactivity ($^3$H) was measured by liquid scintillation counting.

## RESULTS AND DISCUSSION

The clastogenic effect of capsaicin in cultured human lymphocytes is summarized in Table 2. Without S9 activation, the increases in the frequency of total chromosome aberrations induced by capsaicin treatment were concentration-dependent. It is noteworthy that 500 μM capsaicin induced aberrations comparable to that induced by 200 μM of mitomycin C (Table 2). Concurrent with aberrant induction, mitotic indices decreased at all concentrations of capsaicin tested (Fig. 2). Furthermore, capsaicin significantly lowered DNA synthesis in cultured lymphocytes as determined by reduced levels of [$^3$H]thymidine incorporation (Fig. 3). Since early inhibition of [$^3$H]thymidine incorporation has been thought to occur as a result of DNA damage (Painter, 1977), the above finding on the inhibitory effect of capsaicin on DNA replication in human lymphocytes may provide another line of evidence for the genotoxic activity of this compound. To the best of our knowledge, this is the first demonstration of cytotoxic and genotoxic response of human cells to capsaicin.

The addition of hepatic S9 mix lessened the capsaicin-induced clastogenicity (Table 2), an effect possibly due to deactivation of capsaicin through hydrolysis of its amide linkage by liver carboxylesterase activity (Oi *et al.*, 1992; Park and Lee, 1994) or via aliphatic hydroxylation (Lee and Surh, 1986; Surh *et al.*, 1995). The relatively short exposure time (2 h) in cultured lymphocytes containing S9 and capsaicin may also account for the lower clastogenicity than that induced in the cul-

**Table 2.** Comparison of clastogenic activities of capsaicin in cultured human lymphocytes with and without metabolic activation system[a]

| Compound | Conc (μM) | % cells with aberration[b] | Number of aberrations[c] | | | | | | Total aberrations | |
|---|---|---|---|---|---|---|---|---|---|---|
| | | | ctg | ctb | cte | csg | csb | cse | TAG | TA |
| Without S9 mix | | | | | | | | | | |
| $H_2O$ | - | 3 | 2 | 1 | 2 | 4 | 2 | 1 | 12 | 6 |
| DMSO | - | 4 | 3 | 2 | 2 | 6 | 3 | 1 | 17 | 8 |
| Capsaicin | 125 | 9 | 5 | 4 | 4 | 5 | 8 | 2 | 28 | 18 |
| | 250 | 13 | 10 | 12 | 1 | 7 | 13 | 3 | 46 | 29 |
| | 500 | 24 | 6 | 24 | 5 | 8 | 17 | 8 | 68 | 54 |
| Mitomycin C | 200 | 27 | 7 | 23 | 11 | 9 | 12 | 15 | 77 | 61 |
| | 500 | 33 | 5 | 25 | 5 | 20 | 26 | 20 | 101 | 76 |
| With S9 mix | | | | | | | | | | |
| DMSO | - | 3 | 1 | 5 | 0 | 0 | 1 | 0 | 7 | 6 |
| Capsaicin | 125 | 4 | 2 | 5 | 1 | 0 | 0 | 1 | 9 | 7 |
| | 250 | 4 | 2 | 7 | 1 | 0 | 0 | 0 | 10 | 8 |
| | 500 | 7 | 2 | 10 | 0 | 0 | 2 | 1 | 15 | 13 |
| Cyclophosphamide | 50 | 25 | 10 | 20 | 13 | 1 | 13 | 11 | 68 | 57 |

[a]Each compound was incubated with cultured human lymphocytes as described in Materials and Methods. Total 200 metaphase cells were scored for each dose.

[b]Excluding those cells with only chromosome/chromatid gaps.

[c]Abbreviations: ctg, chromatid gap; ctb, chromatid breaks; cte, chromatid exchange; csg, chromosome gap; csb, chromosome breaks; cse, chromosome exchange (dicentric, centric ring, etc.); TAG, total aberrant cells including gaps; TA, total aberrant cells excluding gaps.

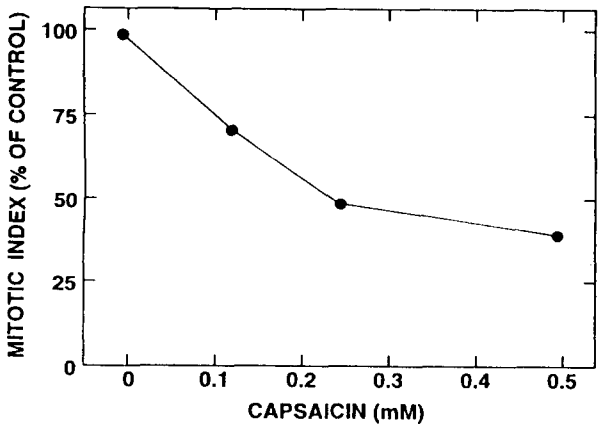


**Fig. 2.** Inhibition of mitotic indices in cultured human lymphocytes treated with capsaicin in the absence of S9 activation.

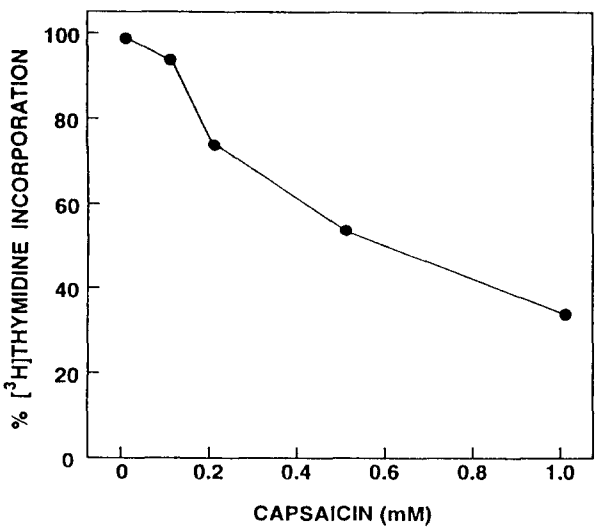


**Fig. 3.** Effect of capsaicin on [$^3$H]thymidine incorporation into human lymphocytes.

tures treated with capsaicin alone. Similar attenuation of genotoxicity by S9 addition was observed with other phenolic substances (Stich *et al.*, 1981). In the presence of S9 mix, capsaicin-treated cells displayed higher mitotic index than those without S9 activation. Furthermore, there was no substantial decrease in the mitotic indices by capsaicin-treatment when S9 was present in the media (data not shown). The presence of S9 mix has also been found to markedly ameliorate the cytotoxicity of certain semisynthetic podophyllotoxin derivatives such as etoposide and teniposide (Larripa *et al.*, 1992). Taken together, the above findings suggest that capsaicin is activated in human lymphocytes *in situ* to exert its clastogenicity. Human lymphocytes have been found to retain some of xenobiotic metabolizing enzyme activities analogous to those found in hepatic microsomes, such as aryl hydrocarbon hydroxylase (Kouri *et al.*, 1981) and cytochrome P450 2E1 (CYP2E1) (Song *et al.*, 1990). Results of recent studies by Gannett *et al.* (1990) suggest that hepatic CYP2E1 is responsible for the activation of capsaicin to an electrophilic metabolite. In view of these findings, capsaicin could be metabolically converted to a mutagen by CYP2E1 activity present in cultured human lymphocytes, but the exact nature of reactive species which might be formed by metabolically competent human lymphocytes is yet to be elucidated.

There are contradictory data on bacterial mutagenicity of capsaicin (*vide infra*). Early studies by Toth *et al.* (1984) revealed low levels of His$^+$ reversion induced by capsaicin in *S. typhimurium* TA98 in the presence of Aroclor 1254-induced rat hepatic S9 mix. Capsaicin containing 20% dihydrocapsaicin exhibited marked mutagenicity in *S. typhimurium* TA98, TA100, and TA 1535 (Nagabhushan and Bhide, 1985 and 1986). However, these findings were not reproduced by other investigators who used synthetic capsaicin of higher purity (Gannett *et al.*, 1988). Later studies by Vinitketkumnuen *et al.* (1991) showed that neither commercial capsaicinoids nor those isolated from chili extracts were mutagenic to *Salmonella typhimurium* TA98, TA 100, and TA1535 when tested with or without S9. Azian and Blevins (1995) have recently reported capsaicin to be mutagenic in the tester strain TA100 in the presence of S9. Few previous studies on capsaicin-induced mutagenesis discussed the identity of ultimate mutagenic species formed from capsaicin. Early work by Lee and Kumar (1980) suggests hepatic microsomal monooxygenase-mediated ring epoxidation as a possible metabolic activation pathway for capsaicin. In line with this idea, Miller *et al.* (1983) have demonstrated the covalent interaction of tritium-labeled capsaicin to tissue macromolecules in the presence of rat liver microsomes fortified with NADPH. An alternate mechanism of metabolic activation of capsaicin would involve the generation of a phenoxy radical intermediate through one electron oxidation catalyzed by peroxidase activity or hepatic microsomal cytochrome P450, probably CYP2E1, as suggested by Lawson and Gannett (1989). Irreversible interaction of the reactive metabolite of capsaicin with the active site(s) of CYP2E1 would lead to the loss of ca-

talytic activity of the same enzyme, which, in turn, may prohibit further activation of not only capsaicin but also other xenobitotics catalyzed by this isoform (Surh *et al.*, 1995). Recent studies by Boersch and co-workers (1991) have revealed the formation of a fluorescence dimer from capsaicin in the presence of peroxidase activity and hydrogen peroxide, lending further support to the possibility of one electron oxidation of capsaicin. The chemical stability or electrophilicity of such reactive species of capsaicin would considerably affect the capsaicin-induced genotoxicity. In addition, the ability of host cells to metabolically activate capsaicin is considered to be another limiting factor for its interaction with nuclear DNA, a critical event leading to mutations. While human lymphocytes have capacity to metabolize capsaicin to mutagenic species, such activation is unlikely to occur in tester strains used for conventional bacterial mutagenicity assays including the Ames-*Salmonella* assay. Therefore, the bacterial mutagenicity of capsaicin would be anticipated to be solely dependent on an external activation system such as S9 mix.

In view of widespread occurrence and frequent consumption of capsaicin in the form of dietary capsicum, the better understanding of its genotoxic effects as well as metabolic fate in humans is crucial. Capsicum is one of the most frequently consumed spices, particularly in South East Asian and Latin American countries where per capita daily intake of capsicum fruits ranges from 2.5 to 15 g (Govindarjan and Sathyanarayana, 1991). The genotoxicity of capsaicin in cultured human lymphocytes together with bacterial mutagenicity data suggest that this dietary phytochemical may have great public health importance. Further epidemiological studies which employ reliable biomarkers are needed to precisely link the genotoxicity of capsaicin to its possible risk in human populations.

## ACKNOWLEDGEMENTS

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## REFERENCES

1. Agrawal, R.C., M. Wiessler, E. Hecker, and S.V. Bhide, (1986): Tumour-promoting effect of chilli extract in BALB/c mice, *Int. J. Cancer* **38:** 689-695.
2. Ames, B.N., (1983): Dietary carcinogens, and anticarcinogens, *Science* **221:** 1256-1264.
3. Azian, A. and R.D. Blevins, (1995): Mutagenicity, and antimutagenicity testing of six chemicals associated with the pungent properties of specific spices as revealed by the Ames *Salmonella/microsome assay. Arch. Environ. Contam, Toxicol.* **28:** 248-258.
4. Boersch, A., B.A. Callingham, F. Lembeck, and D.F. Sharman, (1991): Enzymic oxidation of capsaicin. *Biochem, Pharmacol.* **41:** 1863-1869.
5. Buchanan, R.L., S. Goldstein, and J.D. Budroe, (1981): Examination of chili pepper and nutmeg oleoresin using the *Salmonella*/mammalian microsome mutagenicity assay, *J. Fd. Sci.* **47:** 330-333.
6. Evans, H.J. and M.L. Oiordan, (1975): Human peripheral blood lymphocytes for the analysis of chromosome aberrations in mutagen tests, *Mutat. Res.* **31:** 135-148.
7. Gannett, P.M., D.L. Nagel, P.J. Reilly, T. Lawson, J. Sharpe, and B. Toth, (1988): The capsaicinoids: Their separation, synthesis, and mutagenicity, *J. Org. Chem.* **53:** 1064-1071.
8. Gannett, P.M., P. Iversen, and T. Lawson, (1990): The mechanism of inhibition of cytochrome P450IIE1 by dihydrocapsaicin, *Bioorg. Chem.* **18:** 185-198.
9. Govindarajan, V.S. and M.N. Sathyanarayana, (1991): Capsicum-production, technology, chemistry, and quality. Part V. Impact on physiology, pharmacology, nutrition, and metabolism; structure, pungency, pain, and desensitization sequencies, *CRC Crit. Rev. Food Sci. Nutr.* **29:** 435-474.
10. Hoch-Ligeti, C., (1951): Production of liver tumors by dietary means: effect of feeding chillies (Capsicum frutescence and annum. Linn.), *Acta Unio. Intern. Contra Cancrum.* **7:** 606-611.
11. Jang, J.J. and S.H. Kim, (1988): The promoting effect of capsaicin on the development of diethylnitrosamine-initiated enzyme altered hepatic foci in male Sprague-Dawley rats, *J. Korean Cancer Assoc.* **20:** 1-7.
12. Kouri, R.E., J. Oberdorf, D.J. Slomiany, and C.E. McKinney, (1981): A method for detecting aryl hydrocarbon hydroxylase activities in cryopreserved human lymphocytes, *Cancer Lett.* **14:** 29-40.
13. Larripa, I.B., M.A. Carballo, M.M. Murdry, and M.L. L. de Vinuesa, (1992): Etoposide and teniposide: *in vivo* and *in vitro* genotoxic studies, *Drug Invest.* **4:** 365-375.
14. Lawson, T. and P. Gannett, (1989): The mutagenicity of capsaicin and dihydrocapsaici in V79 cells, *Cancer Lett.*, **49:** 109-113.
15. Lee, S.S. and S. Kumar, (1980): Metabolism *in vitro* of capsaicin, a pungent principle of red pepper, with rat liver homogenates. *In*: Microsomes, Drug Oxidations, and

Chemical Carcinogenesis (M.J. Coon, A.H. Conney, R. W. Estabrook, H.V. Gelboin, J.R. Gillette, and P.J. O'Brien, eds.), Academic Press. Vol. II: 1009-1012.

16. Lee, S.S. and Y.-J. Surh, (1986): ω-Hydroxycapsaicin, a new biotransformation product of capsaicin by rat liver enzyme systems, *J. Prot. Chem.* **5:** 292.
17. Levin, D.E., M. Hollstein, M.F. Christman, E.A. Schwiers, and B.N. Ames, (1982): A new *Salmonella* tester strain (TA102) with A:T base pairs at the site of mutation detects oxidative mutagens, *Proc. Natl. Acad. Sci. USA.* **79:** 7445-7449.
18. Lopez-Carrillo, L., M.H. Avila, and R. Dubrow, (1994): Chili pepper consumption and gastric cancer in Mexico: A case-control study, *Am. J. Epidemiol.* **139:** 263-271.
19. Marnett, L.J., H.K. Hurd, M.C. Hollstein, D.E. Levin, H. Esterbauer, and B.N. Ames, (1985): Naturally occurring carbonyl compounds are mutagens in *Salmonella* tester strain 104, *Mutat. Res.* **148:** 25-34.
20. Maron, D.M. and B.N. Ames, (1983): Revised methods for the *Salmonella* mutagenicity test, *Mutat. Res.* **113:** 173-215.
21. Miller, J.A. and E.C. Miller, (1986): Carcinogens and mutagens that may occur in food, *Cancer* **58:** 1795-1803.
22. Miller, M.S., K. Brendel, T.F. Burks, and I. Glenn Sipes, (1983): Interaction of capsaicinoids with drug-metabolizing systems, *Biochem. Pharmacol.* **32:** 547-551.
23. Nagabhushan, M. and S.V. Bhide, (1985): Mutagenicity of chili extract and capsaicin in short-term tests, *Environ. Mutagen.* **7:** 881-888.
24. Nagabhushan, M. and S.V. Bhide, (1986): Nonmuta genicity of curcumin and its antimutagenic action versus chili and capsaicin, *Nutr. Cancer.* **8:** 201-210.
25. Oi, Y., T. Kawada, T. Watanabe, and K. Iwai, (1992): Induction of capsaicin-hydrolyzing enzyme activity by continuous oral administration of capsaicin, *J. Agr. Food Chem.* **40:** 467-470.
26. Painter, R.B., (1977): Rapid test to detect agents that damage human DNA, *Nature* **265:** 650-651.
27. Park, Y.-H. and Lee, S.-S., (1994): Identification and characterization of capsaicin-hydrolyzing enzymes purified from rat liver microsomes, *Biochem. Mol. Biol. International.* **34:** 351-360.
28. Sbrana, I., L. Zaccaro, D. Lascialfari, I. Ceccherini, and N. Loprieno, (1984): Human lymphocytes assay: cyclophosphamide metbolic activation by S9 system with low cytotoxicity, *Mutat. Res.* **130:** 411-416.
29. Song, B.J., R.L. Veech, and P. Saenger, (1990): Cytochrome P450IIE1 is elevated in lymphocytes from poorly controlled insulin-dependent diabetics, *J. Clin. Endocrinol. Metab.* **71:** 1036-1040.
30. Stich, H.S., M.P. Rosin, C.H. Wu, and W.D. Powrie, (1981): The action of transition metals on the genotoxicity of simple phenols, phenolic acids and cinnamic acids, *Cancer Lett.* **14:** 251-260.
31. Surh, Y.-J., S.H. Ahn, K.-C. Kim, J.-B. Park, Y.W. Sohn, and S.S. Lee, (1995): Metabolism of capsaicinoids: evidence for aliphatic hydroxylation and its pharmacological implications, *Life Sci.* **56:** PL305-PL311.
32. Surh, Y.-J. and S.S. Lee, (1995): Capsaicin, a double-edged sword: toxicity, metabolism and chemopreventive potential, *Life Sci.* **56:** 1845-1855.
33. Surh, Y.-J., R. C.-J. Lee, K.-K. Park, S.T. Mayne, A. Liem, and J.A. Miller, (1995): Chemoprotective effects of capsaicin and diallyl sulfide against mutagenesis or tumorigenesis by vinyl carbamate and N-nitrosodimethylamine, *Carcinogenesis.* 16, in press.
34. Toth, B., E. Rogan, and B. Walker, (1984): Tumori genicity and mutagenicity studies with capsaicin of hot peppers, *Anticancer Res.* **4:** 117-120.
35. Villasenor, I.M. and E.J. de Ocampo, (1994): Clastogenicity of red pepper (*Capsicum frutescens* L.) extracts, *Mutat. Res.* **312:** 151-155.
36. Vinitketkumnuen, U., C. Sasagawa and T. Matsushima, (1991): Mutagenicity study of chili and its pungent principles, capsaicin and dihydrocapsaicin, *Mutat. Res.* **215:** 115 (Abstract No. 81).

# 배양 인형 림프구에 대한 Capsaicin의 유전독성

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## 적 요

사람의 배양 림프구에 대한 고추의 자극성분 **capsaicin**의 염색체이상 유발성을 검토하였다. **Capsaicin (125, 250 및 500 μM)**가 나타내는 세포유전학적 손상을, **chromosome/chromatid aberration**의 빈도증가를 용매대조군과 비교하여 정하였다. 유사분열지수 역시 **capsaicin** 처리 세포에서 농도에 비례하여 감소하였다. 또한 **capsaicin**은 림프구에서 **[$^3$H]thymidine** 취입을 억제하였다. 사람의 림프구에 대한 **capsaicin**의 염색체이상 유발성과 세포독성은 외인성 대사활성 **system**의 첨가 없어도 명확하였다. 이와 같은 발견을 감안할 때 **capsaicin**은 유전독성 물질이고 사람의 건강에 유해하리라고 믿는다.