

Full Length Research Paper

Anti-emetic activity of some members of the family, Euphorbiaceae of Lahore region

Tahira Mughal* and Sana Mahboob

Botany Department, Lahore College for Women University, Jail Road, Lahore, Pakistan.

Accepted 5 August, 2013

The present investigation aimed to evaluate the anti-emetic activity of some members of the family Euphorbiaceae of Lahore region. The selected plants were *Euphorbia prostrata*, *Euphorbia splendens*, *Euphorbia hirta*, *Euphorbia helioscopia*, *Ricinus communis*, *Jatropha integerrima*, *Putranjiva roxburghii* and *Phyllanthus emblica*. Anti-emetic activity was carried out by the preparation of aqueous extract of these plants. Anti-emetic investigations showed that aqueous extracts of *E. prostrata*, *P. roxburghii* and *P. emblica* have high potential to reduce the frequency of retching in CuSO₄ induced emesis in four days old chicks. Frequency of retching after treatment of aqueous extracts of *E. prostrata*, *P. roxburghii* and *P. emblica* were 24.8 ± 0.89 , 17.4 ± 0.89 , 15.2 ± 0.58 , respectively, which statistically proved significant at $p < 0.01$ from the control (87.2 ± 1.46 , 82.6 ± 1.46 , 82.6 ± 1.45 , respectively) values.

Key words: Antiemetic, Euphorbiaceae, CuSO₄.

INTRODUCTION

The use of plants by traditional people has started long time ago, which has laid basis for the discovery of modern medicines. Some years earlier, mankind was well aware of the medicinal characteristics of few plants growing around him (Sofowora, 1982; Hill, 1989). Drug discovery programs have started from the earliest times of mankind's history (Cotton, 1996).

A chemical substance that induces motion sickness, nausea and vomiting is called emetic. Emesis occurs in such cases when a person ingests certain chemical substances such as salt water, mustard water and copper sulphate, zinc sulphate, yellow mercuric subsulphate, alumen and apomorphine. When a toxic substance has been ingested immediately, an emetic is used for their removal from the body (Decker, 1971; Moder and Hurley, 1991).

An anti-emetic is a drug that is widely used to control motion sickness, severe nausea and vomiting. Various types of anti-emetic drugs are used to control nausea and

vomiting. Some of these works on the brain by preventing the activation of the medullar chemoreceptor trigger zone or vomiting centre and other drugs work on the gut by speeding up the rate at which the stomach empties and so help to move food through the intestines more quickly (Zachary et al., 2004).

The family Euphorbiaceae has been selected because many of the members of family Euphorbiaceae has been used as folk medicine in the treatment of different diseases like *Croton tiglium* used as a pain reliever and dry cough (Koche et al., 2010) and *Eclipta alba* (Saxene et al., 1993), *Euphorbia fusiformis* used for Hepatitis (Anusuya et al., 2010), etc.

METHODOLOGY

Selection of plants

Eight plants were selected (*Euphorbia prostrata*, *Euphorbia*

*Corresponding author. E-mail: drtahiramughal@gmail.com or ssass85@yahoo.com. Tel: 042-99203801-8. Ext: 207. Fax: 042-99203810.

splendens, *Euphorbia hirta*, *Euphorbia helioscopia*, *Ricinus communis*, *Jatropha integerrima*, *Putranjiva roxburghii* and *Phyllanthus emblica*) of the family Euphorbiaceae for the study of anti-emetic activity. These plants were selected on the basis of easy approach, easy growth and easy availability and mainly on the basis of ethnomedicinal importance.

Collection of plants

These plants were collected from different areas of Lahore (Lahore College for Women University, Lahore, Lawrence Garden Lahore and Harbanspura, Lahore). These plants were authenticated by Dr. Tahira Aziz Mughal Assistant Professor in Botany Department of Lahore College for Women University, Lahore. Plant specimens were deposited as voucher specimen in Prem Madam Herbarium of Lahore College for Women University, Lahore, for the record and further reference.

Preparation of plant material

Drying and grinding of plants

The plant material was washed with water and dried in shade, then cut into small pieces and ground in an electrical grinder to be obtained in a powder form.

Extraction

Aqueous extract preparation

The crude aqueous extract of the powdered plant material was prepared by using the standard methods (Onyeyili et al., 2001). Twenty grams of the powdered plant material was mixed with 100 ml of distilled water in a 1 L beaker and boiled for 1.5 h. After boiling, it was allowed to cool at room temperature and then filtered by using Whatman 1 filter paper.

Evaporation of solvent

The solvent was removed by rotary evaporator to obtain crude extracts of plant materials. These extracts were stored at 4°C.

Preparation of stock solution

Stock solution was prepared from crude extracts of plants and stock solution was further diluted into different dilutions according to the requirement of the activity either in milligram or microgram.

Anti-emetic activity

Anti-emetic activity of the plant extracts was examined by the methodology of Yang et al. (1999).

Selection of animals

Four days old chicks (male) weighing 35 to 45 g were selected for anti-emetic activity. They are purchased from Tollinton Market, Lahore.

Preparation of animal house for chicks

Chicks were kept in a wire cage. The wire cage was 17 inches in length and 15 inches in width. The chick housing facility was

maintained at standard conditions. Water pot was kept in chick house. Chicks need at least two inches of bedding material beneath them, so straw or dry leaves were spread beneath them.

Feeding routine

Chicks were fed at regular intervals with poultry feeding purchased from Tollinton Market Lahore. The feed was left with them all the time because they will stop eating when they have had enough.

Record of chicks

The information about each chick's group and its age, weight (grams) was recorded at the start and at end of the experiment.

Chemical used to induce the emesis

CuSO₄ was used to induce the emesis. For this purpose 1% CuSO₄ was prepared by dissolving 1 g CuSO₄ in 100 ml distilled water.

Chemical used as diluter

0.9 % saline water drip (Medisol Pvt Ltd, Pakistan) of 1 liter was used.

Preparation of dilutions

Four different concentrations (25, 50, 75 and 100 mg/kg) from crude aqueous plant extract were prepared in saline water.

Induction of emesis

Emesis was induced by 1% CuSO₄ in the chicks orally by 1 ml/20 g body weight.

Experimental plan

The antiemetic activity was determined by calculating the mean decrease in number of retching in contrast with those of the control. All the young male chicks were divided into 12 groups (A, B, C, D, E, F, G, H, I, J, K and L) and groups B, C, D, E, F, G, H, and I were further divided into subgroups. Each group or subgroups had 3 chicks.

Group A

The group A treated as control, was not given any treatment.

Groups B, C, D, E, F, G, H and I

These groups of chicks were administrated with 1% CuSO₄ to induce emesis and after 10 min the number of retching reflexes or emetic action was recorded, and then plant extracts were given in the form of dilution of 25, 50, 75, and 100 mg/kg with the help of a dropper.

Group B

Chicks of group B were administered aqueous extract of *E. prostrata*. This group was further divided into four subgroups.

B₁: Chicks administered with aqueous extract of *E. prostrata* at the dose 25 mg/kg.
 B₂: Chicks administered with aqueous extract of *E. prostrata* at the dose 50 mg/kg.
 B₃: Chicks administered with aqueous extract of *E. prostrata* at the dose 75 mg/kg.
 B₄: Chicks administered with aqueous extract of *E. prostrata* at the dose 100 mg/kg.

Group C

Chicks of group C were treated with aqueous extract of *E. splendens*. This group was further divided into four subgroups.

C₁: Chicks treated with aqueous extract of *E. splendens* at the dose 25 mg/kg.
 C₂: Chicks treated with aqueous extract of *E. splendens* at the dose 50 mg/kg.
 C₃: Chicks treated with aqueous extract of *E. splendens* at the dose 75 mg/kg.
 C₄: Chicks treated with aqueous extract of *E. splendens* at the dose 100 mg/kg.

Group D

Aqueous extracts of *E. hirta* was given to chicks of group D. This group was further divided into four subgroups.

D₁: 25mg/kg aqueous extract of *E. hirta* was given to chicks.
 D₂: 50mg/kg aqueous extract of *E. hirta* was given to chicks.
 D₃: 75mg/kg aqueous extract of *E. hirta* was given to chicks.
 D₄: 100mg/kg aqueous extract of *E. hirta* was given to chicks.

Group E

Therapeutically, aqueous extract of *E. helioscopia* was given to the chicks of group E. This group is also divided into four subgroups (E₁, E₂, E₃, and E₄) on the basis of dosage concentration (25, 50, 75 and 100 mg/kg).

Group F

Chicks of group F received the treatment of aqueous extract of *R. communis*. Group F chicks were further divided into four subgroups (F₁, F₂, F₃, and F₄) on the basis of different dosage concentration. F₁ received the treatment of 25 mg/kg, while F₂, F₃, and F₄ received the dosage of 50, 75 and 100 mg/kg, respectively.

Group G

Chicks of group G received an application of aqueous extract of *J. integerrima*. This group was further divided into four subgroups.

G₁: Chicks received aqueous extract of *J. integerrima* at the dose 25 mg/kg.
 G₂: Chicks received aqueous extract of *J. integerrima* at the dose 50 mg/kg.
 G₃: Chicks received aqueous extract of *J. integerrima* at the dose 75 mg/kg.
 G₄: Chicks received aqueous extract of *J. integerrima* at the dose 100 mg/kg.

Group H

Aqueous extract of *P. roxburghii* was given to chicks of group H. This group was further divided into four subgroups.

H₁: Aqueous extract of *P. roxburghii* at the dose of 25 mg/kg was given to chicks.

H₂: Aqueous extract of *P. roxburghii* at the dose of 50 mg/kg was given to chicks.

H₃: Aqueous extract of *P. roxburghii* at the dose of 75 mg/kg was given to chicks.

H₄: Aqueous extract of *P. roxburghii* at the dose of 100 mg/kg was given to chicks.

Group I

Chicks of group I were treated with methanolic extract of *P. emblica*. This group was further divided into four subgroups.

I₁: Chicks therapeutically treated with 25 mg/kg aqueous extract of *P. emblica*.

I₂: Chicks therapeutically treated with 50 mg/kg aqueous extract of *P. emblica*.

I₃: Chicks therapeutically treated with 75 mg/kg aqueous extract of *P. emblica*.

I₄: Chicks therapeutically treated with 100 mg/kg aqueous extract of *P. emblica*.

Group J

Chicks of group J were administrated 50 mg/kg Motilium or Domperidone (Janssen and Janssen Pakistan (Pvt) Ltd.) which served as positive control.

Group K

125 mg/4 ml Gravinate or Dimenhydrinate syrup (Searle pharmaceutical Pakistan (Pvt) Ltd.) was given to chicks of group K which served as positive control.

Group L

Chicks of group L weretreated with 50 mg/kg Metodine or Diiodohydroxyquinoline which served as positive control.

Dosage administration

After dosage administration, the results were recorded by counting number of retching reflexes for the next 10 min.

Calculation of antiemetic activity

The percent inhibition was calculated by the following formula: Inhibition (%) = $A - B / A \times 100$

Where A is frequency of retching before treatment and B is frequency of retching after plant treatment.

Statistical application

The standard error means (SEM) and statistical significance difference was determined by unpaired student t-test with the help of statistical software SPSS 19.

DISCUSSION

Phytochemical screening showed the presence of alkaloids, phytosterol, phenols, flavonoid, tannins and phlobatannins in the extracts of *E. prostrata*, *E. splendens*, *E. hirta*, *E. helioscopia*, *R. communis*, *J. integerrima*, *P. roxburghii* and *P.s emblica* (Tahira et al., 2010).

Table 1. Anti-emetic effect of aqueous extract of *E. prostrata* on copper sulfate induced emesis in young chicks.

Concentration of plant extract (mg/kg)	Average weight (g)	*Mean $\pm$ S.E.M. of no. of retching/10 min		Inhibition (%)	Remark
		Before plant treatment	After plant treatment		
25	39.5	66.7 $\pm$ 2.03	36.8 $\pm$ 2.03	44.8	Insignificant
50	37.4	72.4 $\pm$ 1.46	34.3 $\pm$ 0.89	52.6	Significant
75	35.8	67.3 $\pm$ 2.03	26.7 $\pm$ 0.67	60.3	Significant
100	40.7	87.2 $\pm$ 1.46	24.8 $\pm$ 0.89	71.5	Significant

*Significantly different from the control value $p < 0.01$.

Table 2. Anti-emetic effect of aqueous extract of *E. splendens* on copper sulfate induced emesis in young chicks.

Concentration of plant extract (mg/kg)	Average weight (g)	*Mean $\pm$ S.E.M. of no. of retching/10 min		Inhibition (%)	Remark
		Before plant treatment	After plant treatment		
25	38.2	56.3 $\pm$ 1.77	33.6 $\pm$ 2.03	40.3	Insignificant
50	42.8	60.4 $\pm$ 1.34	32.7 $\pm$ 1.46	45.8	Insignificant
75	44.5	65.7 $\pm$ 1.77	31.3 $\pm$ 1.77	52.3	Insignificant
100	36.7	66.7 $\pm$ 2.03	25.4 $\pm$ 0.89	61.9	Significant

*Significantly different from the control value $p < 0.01$.

Table 3. Anti-emetic effect of aqueous extract of *E. hirta* on copper sulfate induced emesis in young chicks.

Concentration of plant extract (mg/kg)	Average weight (g)	*Mean $\pm$ S.E.M. of no. of retching/10 min		Inhibition (%)	Remarks
		Before plant treatment	After plant treatment		
25	37.3	65.2 $\pm$ 1.21	43.7 $\pm$ 1.21	32.9	Insignificant
50	35.6	79.3 $\pm$ 1.46	46.4 $\pm$ 1.46	41.4	Insignificant
75	39.8	59.4 $\pm$ 1.21	28.7 $\pm$ 0.89	51.6	Significant
100	42.4	78.2 $\pm$ 1.21	31.3 $\pm$ 0.89	59.9	Significant

*Significantly different from the control value $p < 0.01$.

Four days old chick is a useful animal model selected for anti-emetic effects because this animal possesses acute emesis that is observed in man. This animal also serves as a useful animal for evaluating the involvement of the brain in the observed anti-emetic effects of the extracts (Tijani et al., 2008).

Emesis (nausea and vomiting) is caused by interaction of gastrointestinal system, the vestibular system and the various areas of the brain like chemoreceptor trigger zone (CTZ) in the brain (Gan et al., 2003). Emesis occurred due to copper sulfate, because copper sulphate causes the excitation of visceral afferent nerve fibers of gastrointestinal tract. It has also been observed that the peripheral 5HT₄ plays a major role in copper sulphate induced emesis (Andrews et al., 1990). An aqueous extract of *E. prostrata* exhibited significant inhibition (71.5%) of emesis at the dose of 100 mg/kg (Table 1).

Lower concentrations of aqueous extract of *E. splendens* showed insignificant results but at the dose of 100 mg/kg it showed significant inhibition (61.9%) of emesis (Table 2). 59.9% inhibition of emesis was observed by the therapeutic treatment of aqueous extract

of *E. hirta* at the dose 100 mg/kg (Table 3). An aqueous extract of *E. helioscopia* at the dose of 25, 50, 75 and 100 mg/kg exhibit 23.5, 35.1, 49.8 and 55.2% inhibition of emesis respectively (Table 4). The frequency of retching in young chicks reduced (61%) significantly by the administration of aqueous extract of *R. communis* only at higher concentration (100 mg/kg) (Table 5). An aqueous extract of *J. integerrima* therapeutically reduced the copper sulfate induced emesis in young chicks by increasing the concentration of plant extract (Table 6). Significant inhibition of emesis observed by the application of aqueous extract of *P. roxburghii* even at lower concentration like 25 mg/kg showed 61.7% inhibition of emesis in young chicks (Table 7). An aqueous extract of *P. emblica* at the dose of 25, 50, 75 and 100 mg/kg showed 59.9, 63.7, 70.8 and 81.6 % inhibition of emesis, respectively (Table 8).

The most important findings of the present study are that, all the selected plants significantly reduced the frequency of copper sulphate induced retching in four days old chicks as compared to commercially available medicines: Gravinate, Metodine and Motilium (Table 9).

Table 4. Anti-emetic effect of aqueous extract of *E. helioscopia* on copper sulfate induced emesis in young chicks.

Concentration of plant extract (mg/kg)	Average weight (g)	*Mean $\pm$ S.E.M. of no. of retching/10 min		Inhibition (%)	Remark
		Before plant treatment	After plant treatment		
25	42.7	75.2 $\pm$ 1.46	57.5 $\pm$ 1.16	23.5	Insignificant
50	36.9	71.8 $\pm$ 1.77	46.6 $\pm$ 1.86	35.1	Insignificant
75	39.4	78.4 $\pm$ 1.46	39.3 $\pm$ 0.89	49.8	Significant
100	41.7	76.5 $\pm$ 1.21	34.2 $\pm$ 0.89	55.2	Significant

*Significantly different from the control value $p < 0.01$.**Table 5.** Anti-emetic effect of aqueous extract of *R. communis* on copper sulfate induced emesis in young chicks.

Concentration of plant extract (mg/kg)	Average Weight (g)	*Mean $\pm$ S.E.M. of no. of retching/10 min		Inhibition (%)	Remark
		Before plant treatment	After plant treatment		
25	40.6	78 $\pm$ 1.53	55 $\pm$ 1.77	29.4	Insignificant
50	35.3	75 $\pm$ 1.74	46.4 $\pm$ 1.77	38.2	Insignificant
75	44.8	79.7 $\pm$ 1.23	41.7 $\pm$ 1.86	47.7	Insignificant
100	40.5	63.4 $\pm$ 1.21	24.7 $\pm$ 0.89	61	Significant

*Significantly different from the control value $p < 0.01$.**Table 6.** Anti-emetic effect of aqueous extract of *J. integerrima* on copper sulfate induced emesis in young chicks.

Concentration of plant extract (mg/kg)	Average weight (g)	*Mean $\pm$ S.E.M. of no. of retching/10 min		Inhibition (%)	Remark
		Before plant treatment	After plant treatment		
25	36.8	77.5 $\pm$ 1.76	41.4 $\pm$ 1.21	46.5	Insignificant
50	37.4	70.7 $\pm$ 1.21	29.2 $\pm$ 0.77	58.6	Significant
75	43.2	77.8 $\pm$ 1.86	28.2 $\pm$ 0.89	63.7	Significant
100	40.5	87.6 $\pm$ 1.77	31.3 $\pm$ 0.89	64.2	Significant

*Significantly different from the control value $p < 0.01$.**Table 7.** Anti-emetic effect of aqueous extract of *P. roxburghii* on copper sulfate induced emesis in young chicks.

Concentration of plant extract (mg/kg)	Average weight (g)	*Mean $\pm$ S.E.M. of no. of retching/10 min		Inhibition (%)	Remark
		Before plant treatment	After plant treatment		
25	36.5	67 $\pm$ 2.31	25.7 $\pm$ 0.89	61.7	Significant
50	40.8	78.4 $\pm$ 1.46	25.4 $\pm$ 0.89	67.6	Significant
75	43.4	88.3 $\pm$ 1.21	25.7 $\pm$ 0.89	70.8	Significant
100	44.3	82.6 $\pm$ 1.46	17.4 $\pm$ 0.89	78.9	Significant

*Significantly different from the control value $p < 0.01$.**Table 8.** Anti-emetic effect of aqueous extract of *P. emblica* on copper sulfate induced emesis in young chicks.

Concentration of plant extract (mg/kg)	Average weight (g)	*Mean $\pm$ S.E.M. of no. of Retching/10 min		Inhibition (%)	Remark
		Before plant treatment	After plant treatment		
25	37.8	78.4 $\pm$ 1.21	31.3 $\pm$ 0.89	59.9	Significant
50	38.5	77.8 $\pm$ 1.86	28.2 $\pm$ 0.89	63.7	Significant
75	39.8	88.3 $\pm$ 1.21	25.7 $\pm$ 0.89	70.8	Significant
100	41.4	82.6 $\pm$ 1.45	15.2 $\pm$ 0.58	81.6	Significant

*Significantly different from the control value $p < 0.01$.

Table 9. Anti-emetic effect of commercial medicines on copper sulfate induced emesis in young chicks.

Commercial Medicines	Average weight (g)	*Mean $\pm$ S.E.M. of no. of Retching/10 min		Inhibition (%)	Remark
		Before plant treatment	After plant treatment		
Motilium (50 mg/kg)	35.7	87.6 $\pm$ 1.76	17.4 $\pm$ 0.89	80.9	Significant
Gravinate (125 mg/4 ml)	44.6	65.7 $\pm$ 1.76	11.7 $\pm$ 0.89	82.2	Significant
Metodine (50 mg/kg)	37.9	66.7 $\pm$ 2.03	10.6 $\pm$ 0.89	84.6	Significant

*Significantly different from the control value $p < 0.01$.

These medicines showed anti-emetic activity by acceleration of gastrointestinal tract movement (Akita et al., 1998).

The observed anti-emetic activity of plant extracts in the present study may be attributed to its phytochemical (alkaloids, phytosterol, phenols, flavonoid, tannins and phlobatannins) constituents, like in previous studies, shogaol and gingerols isolated from *Zingiber officinale* showed the anti-emetic activity (Akita et al., 1998) and diarylheptanoids isolated from *Alpinia officinarum* (Itokawa et al., 1981a, 1985b; Uehara et al., 1987), *Alpinia conchigera*, *Alpinia oxyphylla* (Itokawa et al., 1982c; Shoji et al., 1984), *Alpinia bleparocalyx* (Kadota et al., 1994), and *Curcuma comosa* and *Curcuma xanthorrhiza* (Uehara et al., 1987) showed highest anti-emetic activity. These plants have been used in Chinese traditional medicine as the anti-emetics.

Therefore, it is concluded that these plants *E. prostrata*, *E. splendens*, *E. hirta*, *E. helioscopia*, *R. communis*, *J. integerrima*, *P. roxburghii* and *P. emblica* showed significant anti-emetic activity and thus provides the basis for their use in traditional or folk medicines for the treatment of emesis.

REFERENCES

- Andrews PLR, Davis CJ, Bingham S, Davidson HIM, Hawthorn J, Maskell L. (1990). The abdominal visceral innervations and the emetic reflex: Pathways, pharmacology, and plasticity. *Can. J. Physiol. Pharmacol.* 68:325-345.
- Anusuya N, Raju K, Manian S (2010). Hepatoprotective and toxicological assessment of an ethnomedicinal plant *Euphorbia fusiformis* Buch.-Hamex D. Don. *J. Ethnopharmacol.* 127:463-467.
- Cotton CM (1996). *Ethnobotany: Principle and Application*. John Wiley and Sons, New York. p. 399.
- Decker WJ (1971). "In Quest of Emesis: Fact, Fable, and Fancy". *Clin. Toxicol.* 4(3): 383-387.
- Gan TJ, Meyer T, Apfel CC (2003). Consensus guidelines for managing post operative nausea and vomiting. *Anaesth. Analg.* 97:62-71.
- Hill AF (1989). *Economic Botany: a Text Book of Useful Plants and Plant products*, second ed. Mc Graw Hill Book Company, Inc., New York. p. 560.
- Koche D, Shirsat R, Imran S, Bhadange DG (2010). Phytochemical Screening of Eight Traditionally Used Ethnomedicinal Plants from Akola District (MS) India. 1:3.
- Moder KG, Hurley DL (1991). "Fatal hyponatremia from exogenous salt intake: report of a case and review of the literature". *Mayo Clin. Proc.* 65(12):1587-1594.
- Onyeyili PA, Nwosa CO, Amin JD, Jibike JI (2001). Anthelmintic activity of crude aqueous extract of *Nauclea latifolia* stem bark against ovine nematodes. *Fitoterapia.* 72:12-21.
- Saxene AK, Singh B, Anand KK (1993). Hepatoprotective effects of *Eclisa alba* on subcellular levels in rats. *J. Ethnopharmacol.* 40(3):155-161.
- Sofowora A (1982). *Medicinal Plants and Traditional Medicinal in Africa*. Wiley chichester, West Sussex and New York. pp. 256-258.
- Tahira M, Mamona A, Saddique Z, Qureshi S, Mahboob S (2010). Phytochemical and Pharmacognostical Evaluation of Euphorbiaceae Species from Lahore Region, Pakistan. *J. Appl. Pharm.* 3(2):79-85.
- Tijani A, Okhale Y, Oga SE, Tags FE, Salawu OA, Chindo BA (2008). Anti-emetic activity of *Grewia lasiodiscus* root extract and fractions. *Afr. J. Biotech.* 7(17):3011-3016.
- Yang Y, Kaoru K, Kiyotaka K, Kunio T, Takaki T, Yoshiki N, Kazuo W (1999). Two Novel Anti-emetic Principles of *Alpinia katsumadai*. *J. Nat. Prod.* 62:1672-1674.
- Zachary AF, Robert DS, Austin GB (2004). Practical Selection of Antiemetics. *Am. Fam. Phys.* 69(5):1169-1174.