

Tc^{99m}-RENAL IMAGING AGENT - THE PREPARATION AND COMPARATIVE CLINICAL EVALUATION

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ABSTRACT

Radionuclide Tc^{99m} DTPA (Diethylenetriaminepenta Acetic Acid) renal imaging is being used to assist in the evaluation of overall GFR, the separate GFR, the intra-renal transit time, the cortical transit time, response to frusimide injection, diagnosis of ATN and rejection in renal transplant cases. A study was conducted at PINSTECH in order to prepare DTPA kit locally and evaluate the labeling efficiency as well as the invitro and invivo stability of Tc^{99m} DTPA preparation. The results were comparable with those of imported Renal imaging (pentetate-II Technetium 99m) agent. The shelf life of the kit at room temperature recorded is around 3 months, the labeling efficiency with Tc^{99m} pertechnetate is more than 99% and the fraction of hydrolyzed Tc^{99m} recorded is less than 1%. On clinical trials no artifacts were seen on scintigraphic images (JPMA 40:185, 1990).

INTRODUCTION

Tc^{99m} DTPA has been described as the best kidney imaging agent¹⁻³ and is in use in our country for the past several years. But as the reagent has to be imported from U.K. in the form of freeze dried kit⁴ the cost of the kits constitutes a major fraction of the recurring expenditure borne by nuclear medicine departments. The expenses can be reduced considerably by preparing them locally. A procedure for the preparation of Tc^{99m} DTPA kit adopted at PINSTECH is submitted and the steps taken to ensure the quality control of these kits are also described. A comparative study was also conducted over a selected group of normal volunteers and in renal disorder patients with locally prepared DTPA kits as well as the imported ones (Amersham UK) in order to evaluate their clinical efficiency. There is controversy about the stability of these kits⁵ therefore radiochemical purity and labeling efficiency of these kits at different time and temperature were studied in detail to check the efficiency, stability and shelf life.

MATERIAL AND METHODS

A stock solution (A) of DTPA (Fluka-750 mg) in sterile distilled water (60 ml) was prepared by raising the pH to 7.0 with NaOH. A solution B (20 ml) of SnCl₂ 2H₂O (E. Merck) (800 mg) in HCL was also prepared. With rapid stirring sol. B (1 ml) was added to sol. A. pH was readjusted to 6.8 and volume was brought to 75 ml with sterile distilled water. 1.0 ml aliquot after passing through 0.22 micrometer millipore was dispensed in 70 vials and freeze dried for 48hrs. The vials were then sealed under saline as solvents. 1 cm strips were cut and counted in Gamma counter to calculate activity at different retention values. In order to check stability DTPA was mixed with reducing agent, labeling was carried out on DTPA in solution form, in freeze dried form and at different time intervals (Table-I).

Table 1. Stability of DTPA (in solution form and kit form) after labelling with Tc^{99m} .

S. No.	Time after Labelling	%Activity		
		Labelled compound	Hydrolysed	Free TcO_4
1..	1H	99%	1%	1%
2.	2H	99%	1%	1%
3.	3H	99%	1%	1%
4.	4H	99%	1%	1%
5.	5H	99%	1%	1%
6.	6H	99%	1%	1%
7.	24H	99%	1%	1%
8.	Labelling of stock solution after 24 H	99%	1%	1%
9.	Labelling of stock solution after 48 H	90.1%	6.9%	3%
10.	1 H (DTPA Amersham)	99%	1%	1%

RESULTS AND DISCUSSION

Results shown in Table 1 and Figures 1,2,3,4

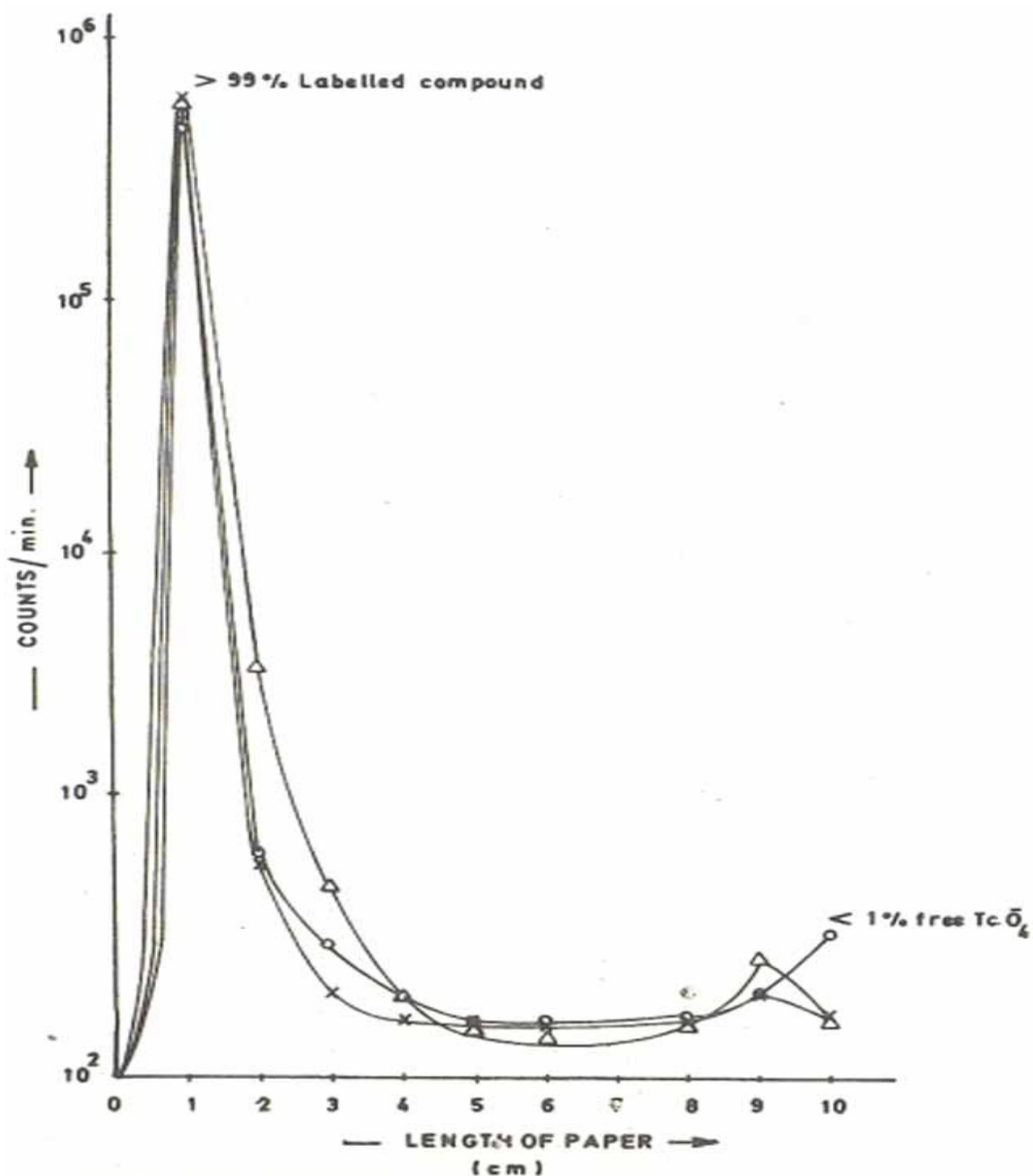


Figure 1. Labelling yield of DTPA freeze dried kit. Paper chromatography (Solvent : Acetone). Rf Labelled compound = 0, Free TcO_4 = 1, Time 1.0 hr = x, 2.0 hrs = o, 3.0 hrs = Δ

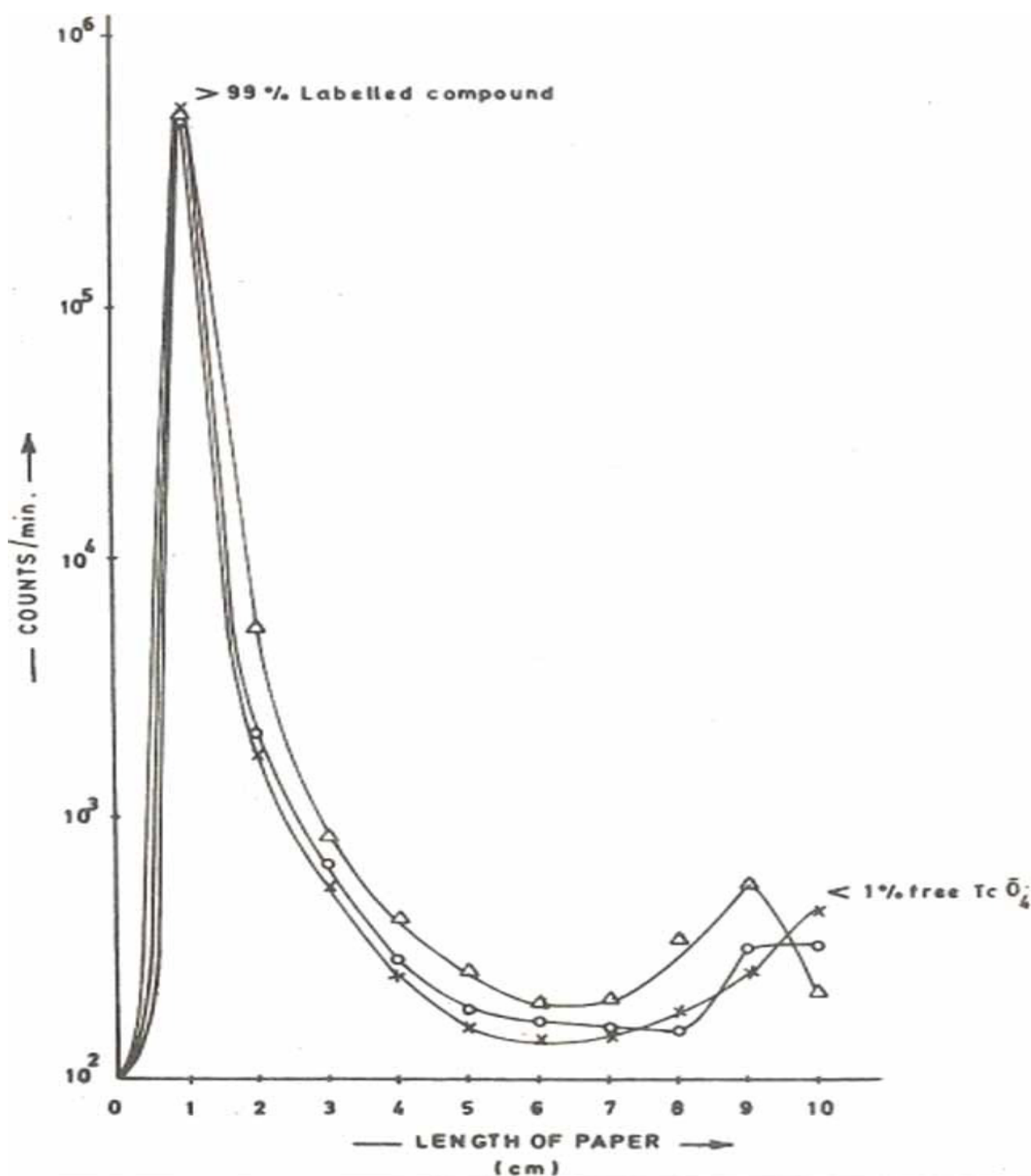


Figure 2. Labelling yield of DTPA freeze dried kit. Paper Chromatography (Solvent: Acetone). Rf-Labelled compound = 0, free $TcO_4 = 1$, Time 4.0 hrs = x, 5.0 hrs = o, 6.0 hrs = Δ.

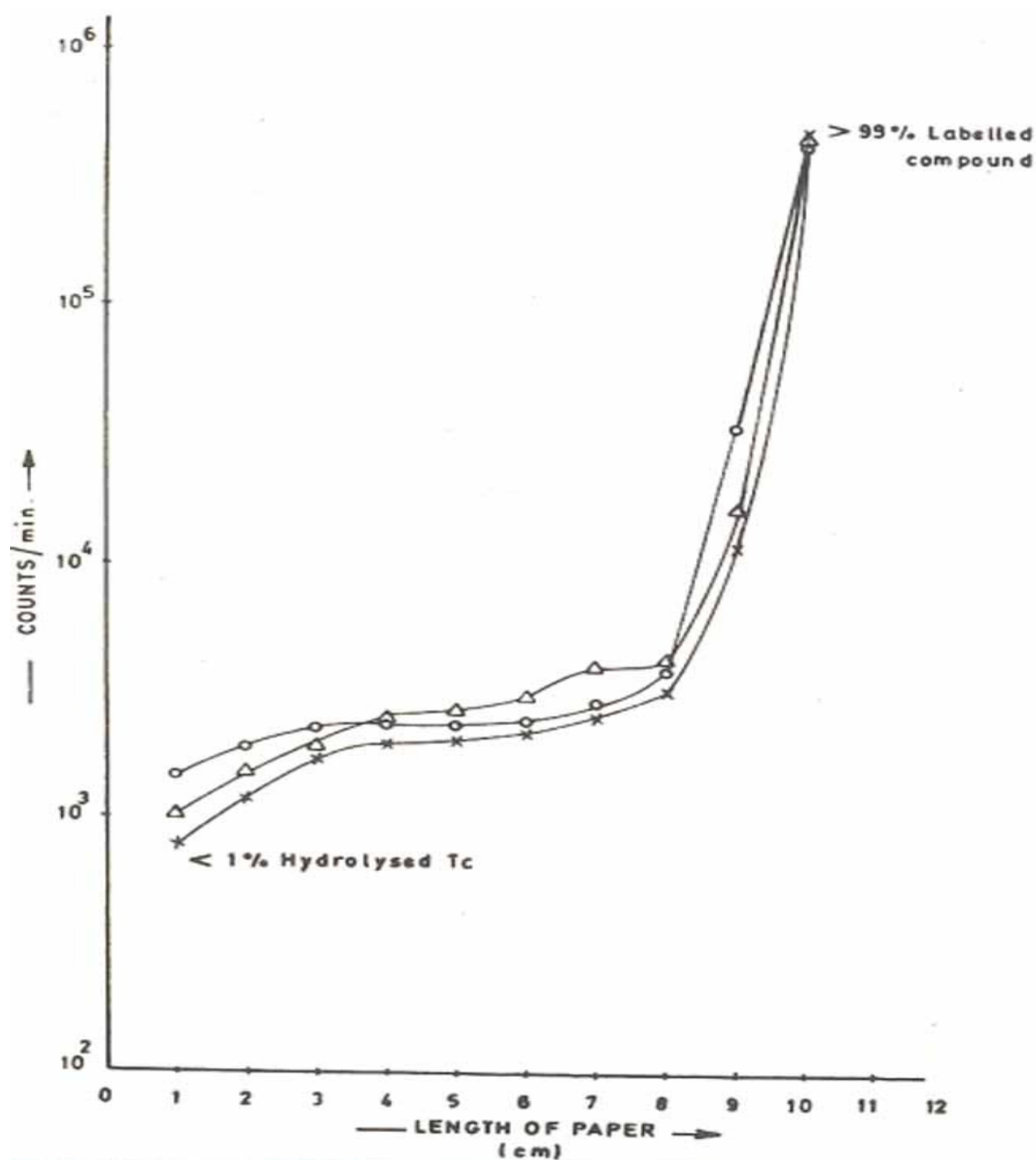


Figure 3. Labelling yield of DTPA freeze dried kit. Paper Chromatography (Solvent : Saline). Rf-Labelled compound = 1, Hydrolysed Tc = 0, Time 1.0 hrs = x, 2.0 hrs = ○, 3.0 hrs = Δ

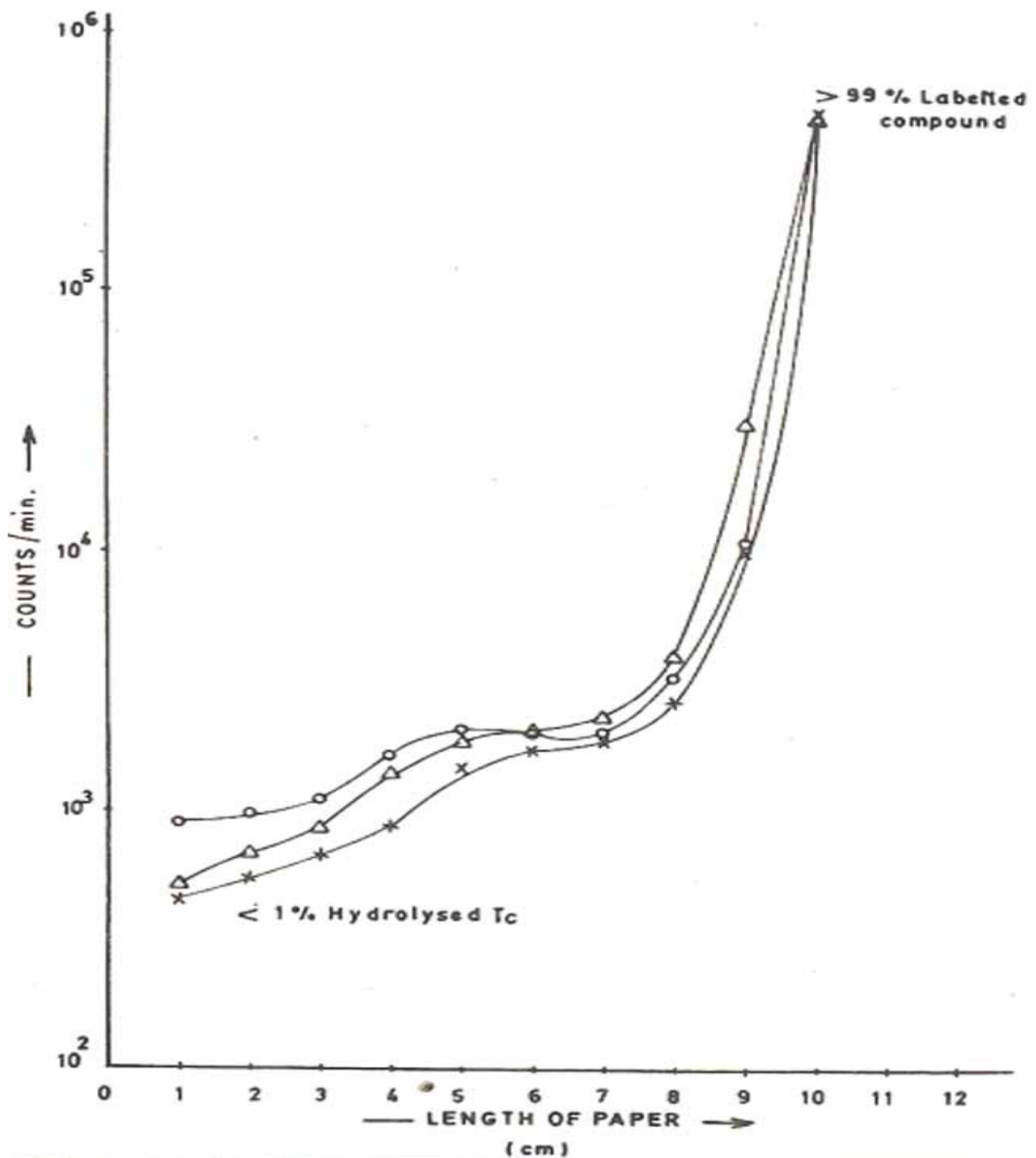


Figure 4. Labelling yield of DTPA freeze-dried kit. Paper Chromatography (Solvent: Saline). R_f -Labelled compound = 1, Hydrolysed Tc = 0, Time 4.0 hrs = x, 5.0 hrs = o, 6.0 hrs = Δ

demonstrate labeling efficiency to be more than 99% which is comparable to that of imported kit (Amersham 'UK). The amount of free pertechnetate and hydrolyzed Technetium recorded is less than 1%. There has been some controversy about the stability of these kits⁵. We found (Figure 5)

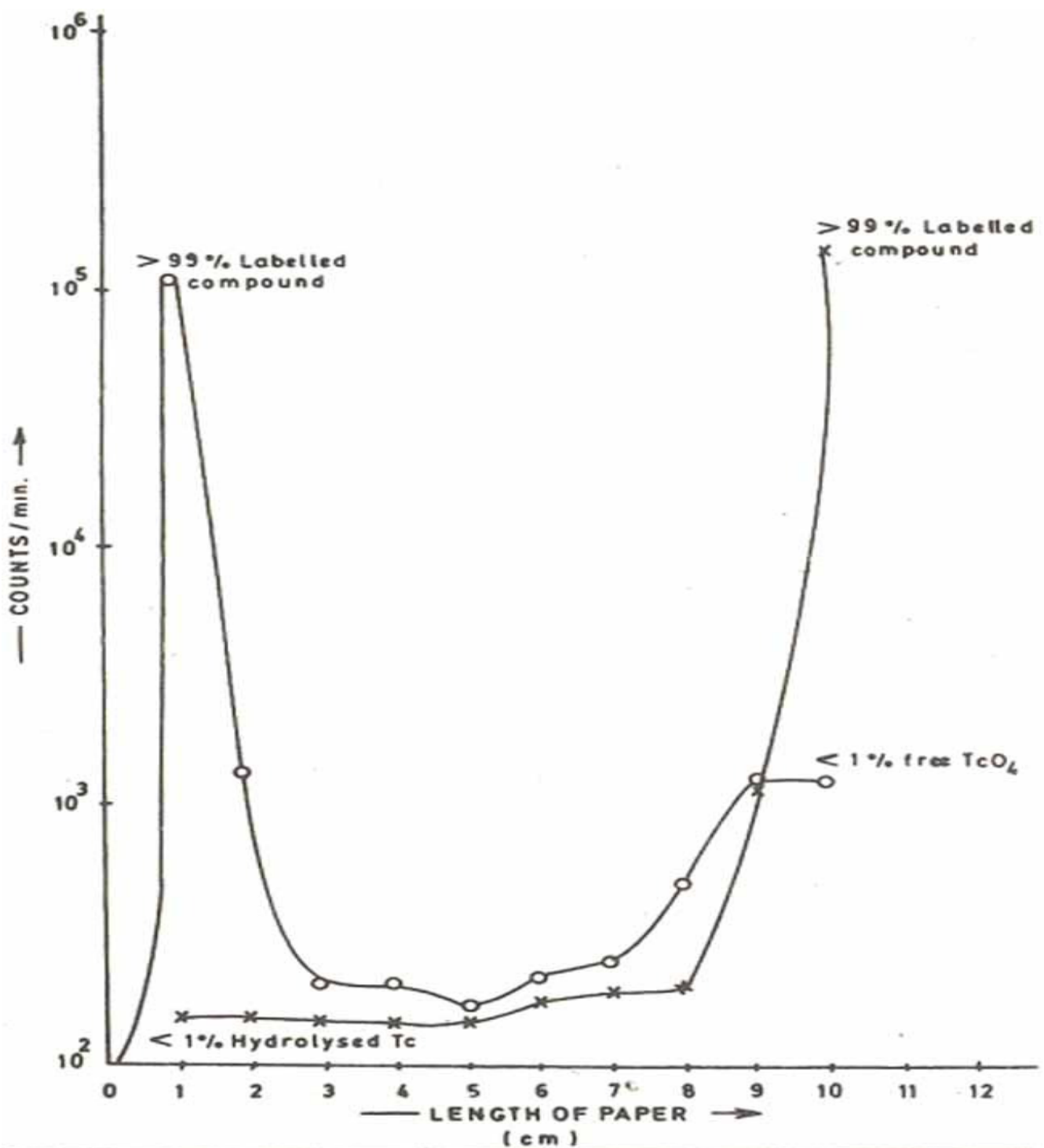


Figure 5. Labelling yield of DTPA freeze dried kit (after 24 hours). Paper Chromatography. (Solvent: Acetone O, Solvent: Saline x). Rf- Labelled compound = 0 (Acetone). Free TcO₄ = 1 (Acetone). Hydrolysed Tc = 0 (Saline).

that the kit containing reducing agent and NaTcO₄-99m (after labeling is stable upto 24 hrs., whereas literature⁵ value is 6 hrs. Similarly our results (Figures 6,7)

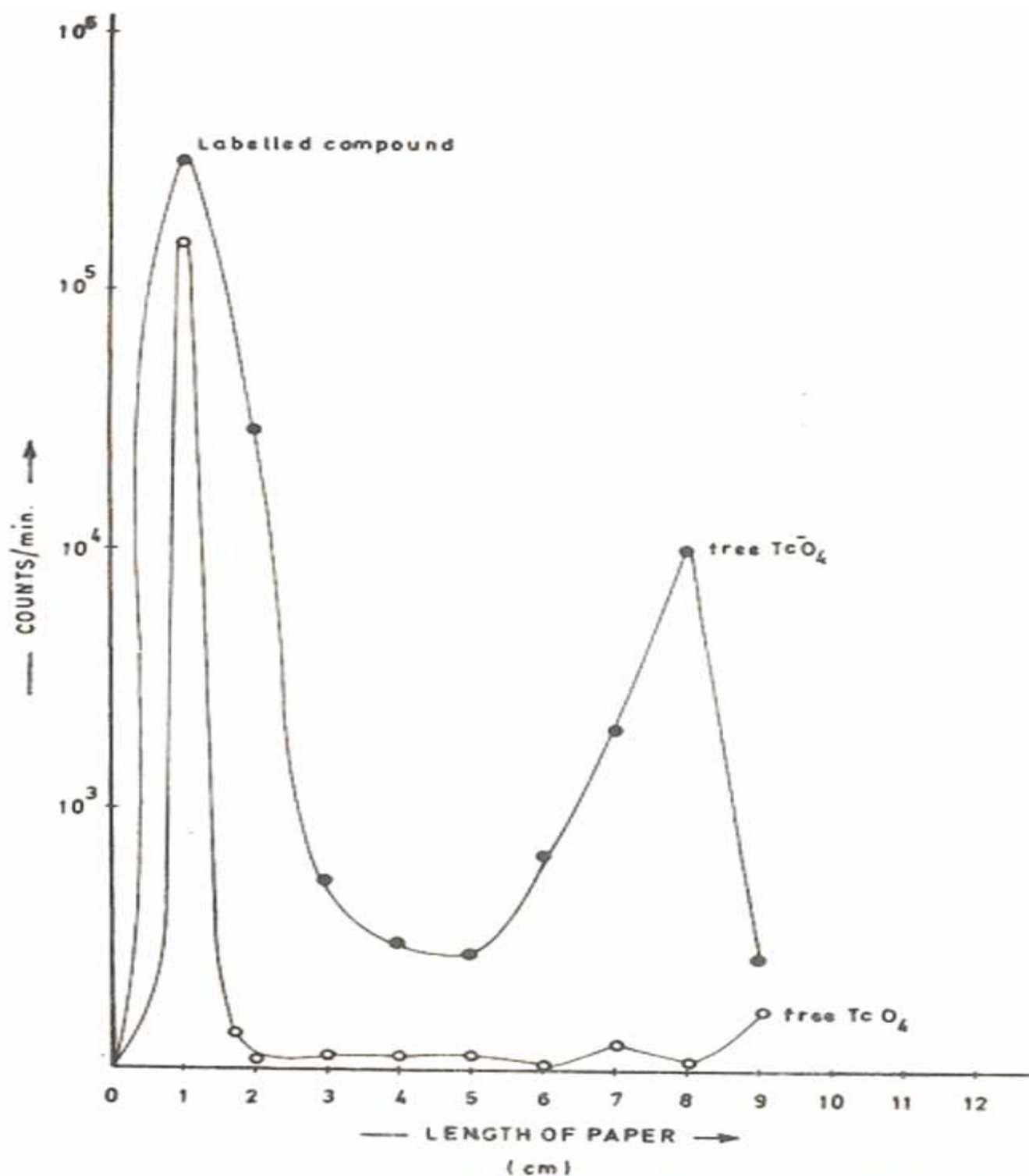


Figure.6 Labelling yield of DTPA solution kit (after 24 & 48 hrs). Paper Chromatography (Solvent: Acetone). R_f-Labelled compound = 0, free TcO₄⁻ = 1, Time 24 hrs = 0, 48 hrs = .

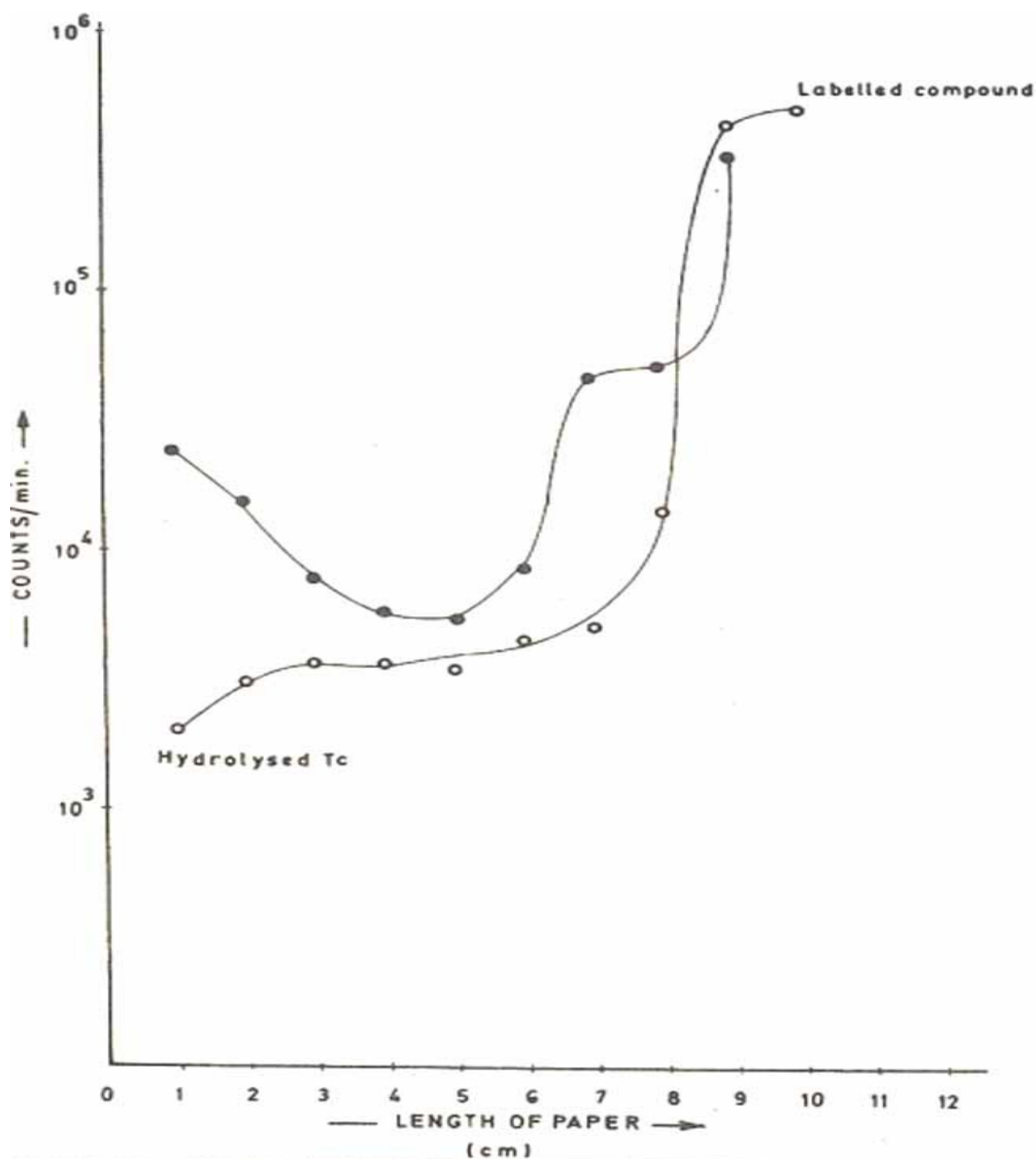


Figure 7. Labelling yield of DTPA kit solution (after 24 to 48hrs). Paper Chromatography (solvent. Saline). R_f -Labelled compound = 1, Hydrolysed Tc = 0, Time 24 hrs = ○, 48 hrs = ●.

showed that DTPA in the stock solution state (with reducing agent) is also stable upto 24 hrs. at 5°C while labeling of this stock solution with TCo₄ after 48 hrs gave free TC0₄ 6.9% and hydrolysed 3%. Stability of the DTPA kits in the freeze dried form kept at 5°C and 20°C has also been studied (Figures 8-10).

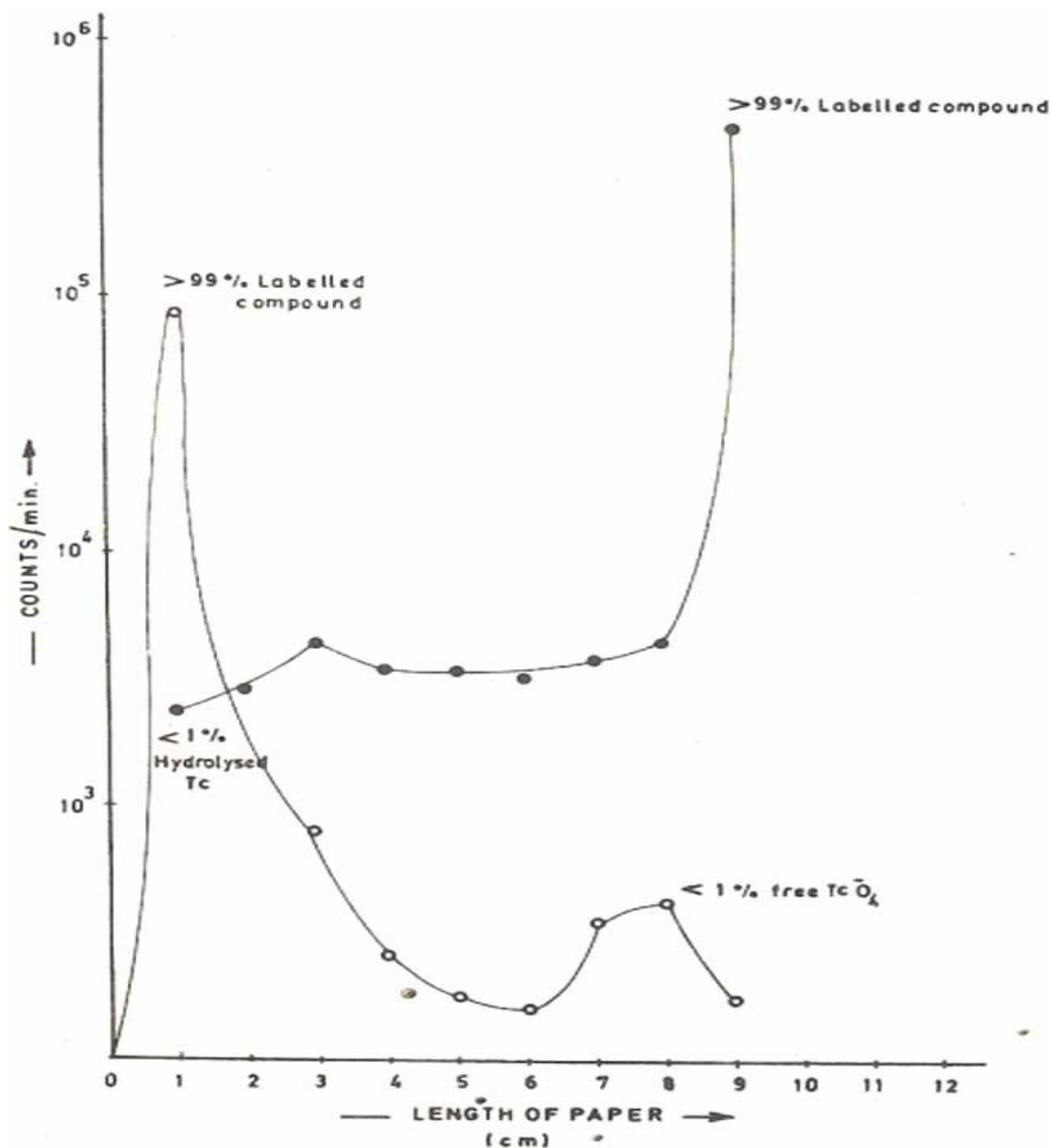


Figure 8. Labelling yield DTPA freeze dried kit (after 3 months) at 5°C. Paper Chromatography (Solvent: Acetone 0, Solvent: Saline ●). Rf-Labelled compound = 0 (Acetone), Rf-Labelled compound = 1 (Saline), free TcO₄ = 1 (Acetone), Hydrolysed Tc = 0 (Saline).

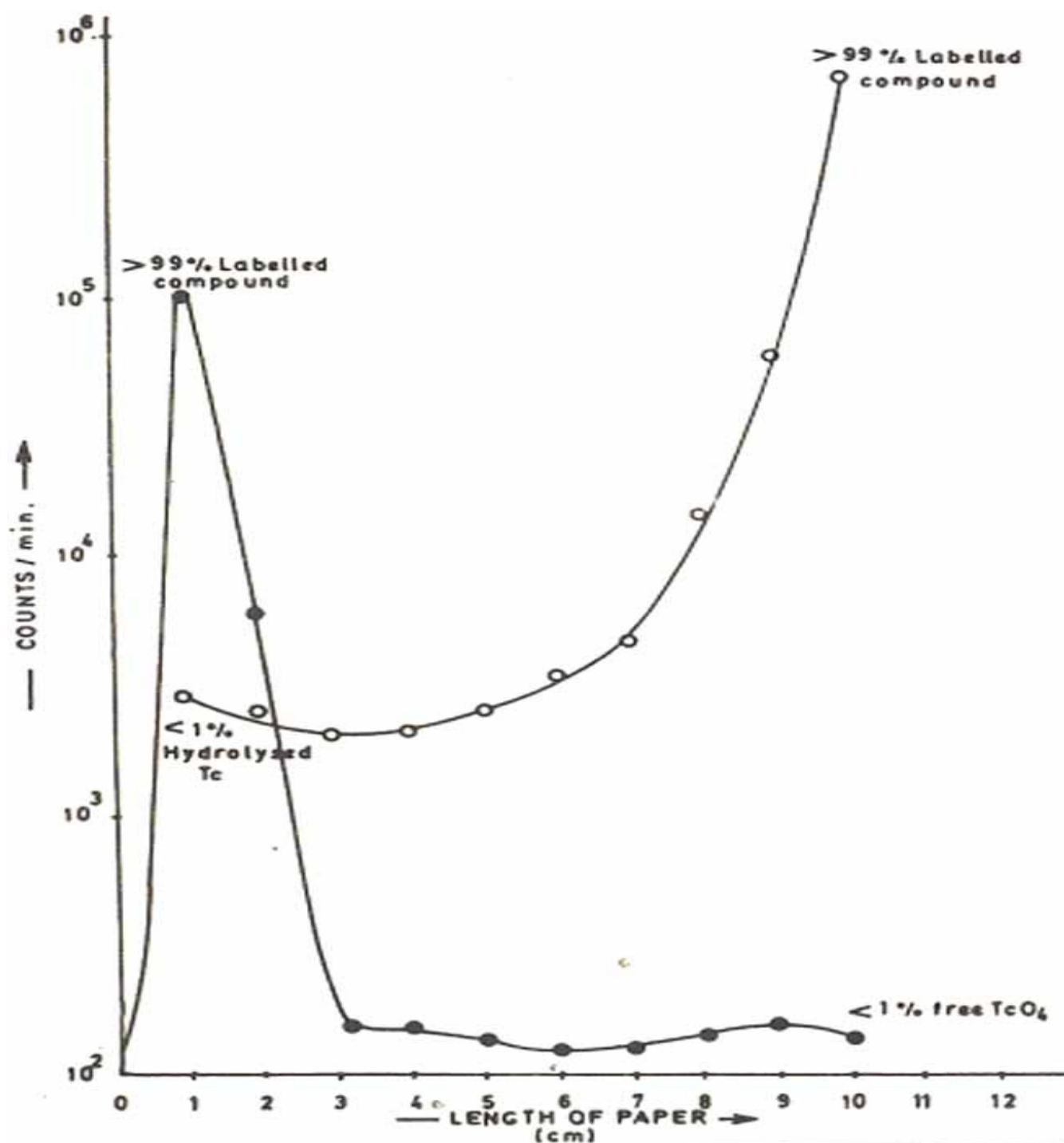


Figure 9. Labelling yield of DTPA freeze dried kit (after 3 months kept at room temperature). Paper chromatography, (Solvent: Acetone = ●, Solvent: Saline = ○. Rf- Labelled compound = 0 (Acetone), Rf-Labelled compound = 1 (Saline), free TcO_4 = 1 (Acetone), Hydrolysed Tc = 0 (Saline).

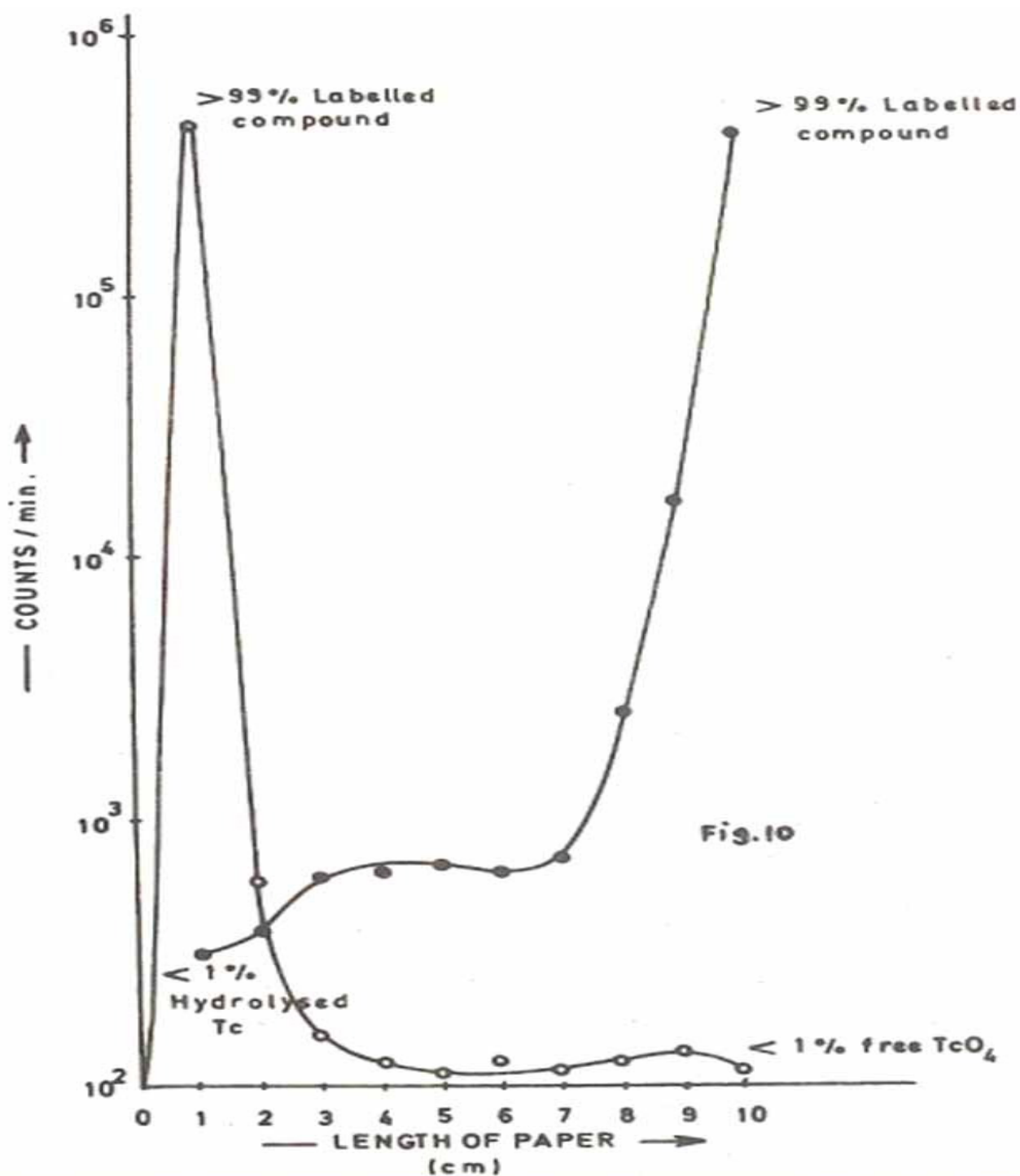


Figure 10. Labelling yield of DTPA (Amersham) kit. Paper Chromatography (Solvent: Acetone O, Solvent; Saline ●). Rf-Labelled compound = 0 (Acetone), Rf-Labelled compound = 1 (Saline) free TcO₄ = 1 (Acetone), Hydrolysed Tc = 0 (Saline).

Therefore shelf life of the kit at room temperature can easily be given upto 3 months. A clinical comparative study was also performed in order to evaluate the invivo stability of Tc^{99m} DTPA preparations. The Tc^{99m} was obtained from a Mo-Tc^{99m} generator (Amersham UK). The equipment used was a large field of view gamma camera (Scintatronix UK) coupled with a general purpose high

resolution low energy collimator. The camera was interfaced to an on-line computer (NoVa 4c). The study group included normal volunteers, normal functioning transplant and transplant with ATN and rejection. These groups were studied under similar conditions at an interval of 24 hrs with Tc^{99m} pentetate II Amersham kit and Tc^{99m} DTPA PINSTECH kit. Tc^{99m} renal imaging agent injected in bolus dose of 5 mCi. The study was recorded on a computer at a frame rate of one frame per second for the first 30 sec and then 30 sec frames for the next 30 min. Processing of the study was performed by drawing region of interest over the kidneys background and bladder areas. In case of transplant kidneys additional area of interest was drawn over the iliac artery distal to transplant. Time activity curves for these regions were generated from derived data and curves “up slope” (CPS/Sec), “peak” (min) and “down slope” (CPS/Sec) were calculated. Thyroid activity was also recorded in each case. On analysis of these time activity curves results were comparable with those of imported kits (Table II).

Table II. Computer generated curve analysis of imported (Amersham-pentetate II, Technetium-99m agent) Kit with locally prepared (PINSTECH) DTPA Kit at an interval of 24 hours, based on comparable Biochemical values.

Sl. No.	Study group	Time lapsed between Injection and DTPA preparation (hr)	Tc ^{99m} Dose (mCi)	COMPUTER GENERATED RENOGAM CURVE ANALYSIS											
				Amersham Renal Imaging Kit (UK)						PINSTECH Renal Imaging Kit					
				Upslope of Curve (CPS/Sec)	Peak (Min)	Down slope (SPS/Sec)	Perfusion Index (PI) (%)	Appearance of activity in Urinary Bladder (Min)	Thyroid activity	Upslope of Curve (CPS/Sec)	Peak of Curve (Min)	Down slope (SPS/Sec)	Perfusion Index (PI) (%)	Appearance of activity in Urinary Bladder (Min)	Thyroid activity
	Normal ¹⁰	1	5	1.75±0.21	4.30±1.20	-1.12±0.40	—	4.50±0.80	Nil	1.80±0.24	3.50±0.50	-1.14±0.35	—	4.0±1.0	Nil
		1.30	5	1.70±0.30	5.10±1.0	-1.20±0.05	—	5.20±1.07	Nil	1.67±0.30	4.30±1.10	-1.07±0.07	—	4.45±1.02	Nil
		2.30	5	1.65±0.25	4.0±0.87	-1.01±0.08	—	4.12±0.97	Nil	1.42±0.29	4.70±1.0	-1.13±0.16	—	4.30±1.02	Nil
	Normal ³ (Transplant)	2	5	1.10±0.5	4.12±1.05	-0.78±0.20	110±30	4.30±1.11	Nil	1.15±0.10	4.30±1.0	-0.95±0.15	100±20	4.45±1.05	Nil
	Atn ⁴ (Transplant)	2	5	1.0±0.20	10.30±1.20	-0.03±0.01	240±20	11.0±2.0	Nil	1.25±0.25	11.45±1.3	-0.06±0.02	190±30	7.45±1.45	Nil
	Rejection ⁴	2	5	0.72±0.10	7.30±2.0	-0.04±0.02	330±30	9.45±1.45	Nil	1.0±0.20	8.1±2.30	-0.03±0.02	312±40	9.0±1.40	Nil

The scintigraphic images (Figures 11,12)

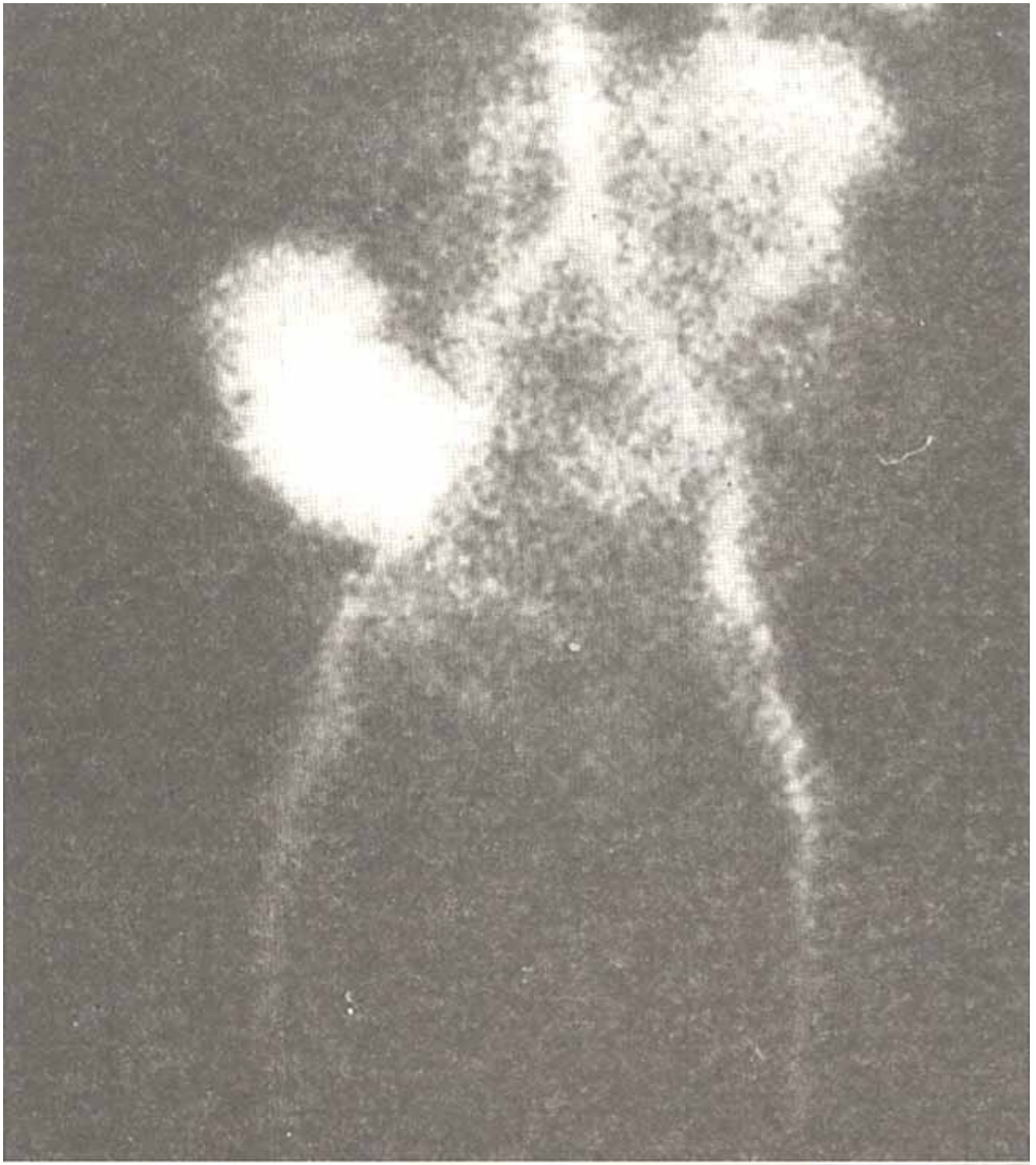


Figure 11. Normal Tc^{99m} DTPA (PINSTECH) image of Renal Transplant.

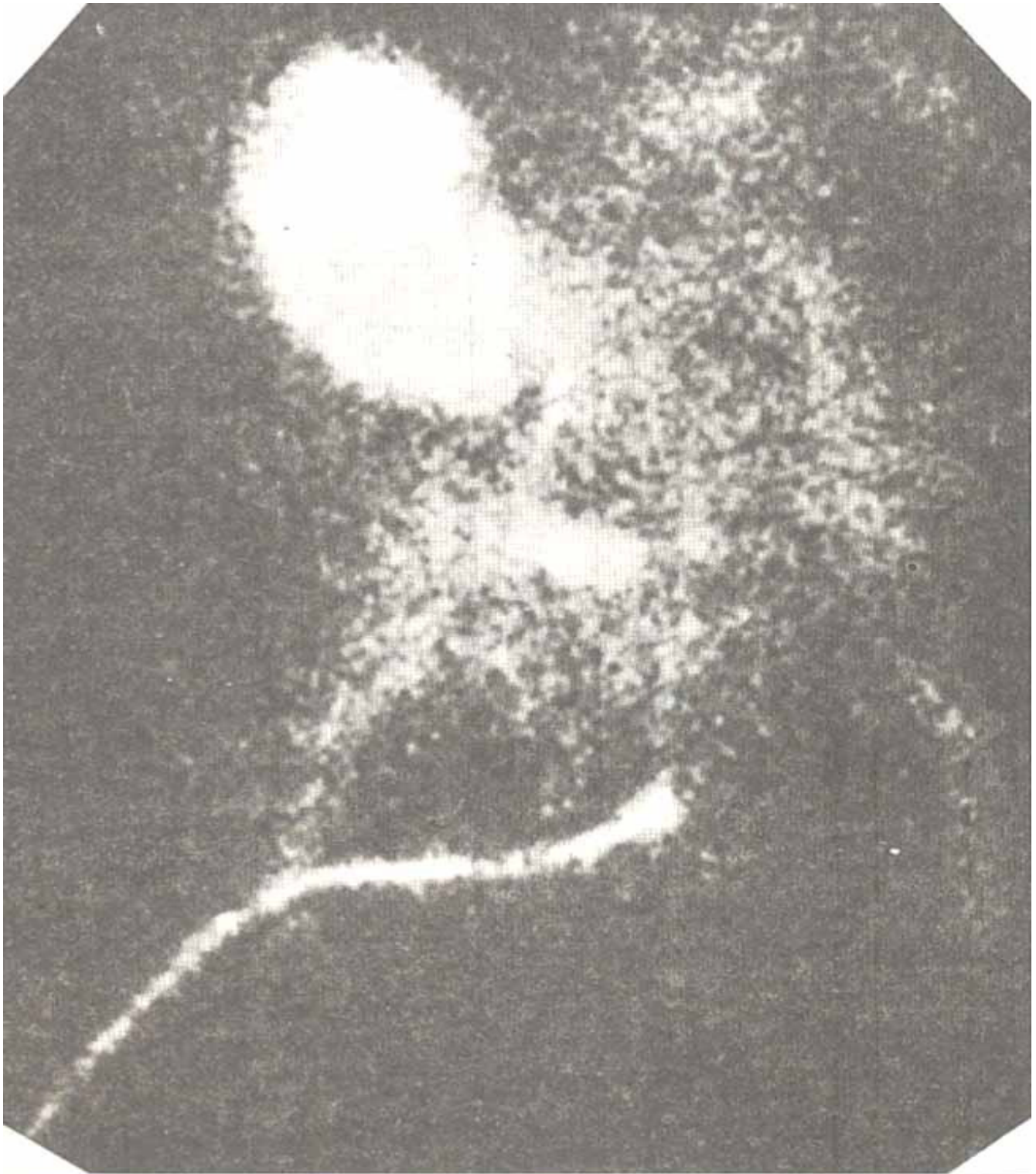


Figure 12. Normal Tc^{99m} DTPA (Amersham-pentetate II) image of renal Transplant.

also showed perfect labeling, stability of Tc^{99m} DTPA preparation with no image artifact.

CONCLUSION

Regular production of these kits locally has resulted into saving of foreign exchange and the facility of radionuclide renal imaging has been extended to large number of patients.

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