CHAPTER 4

Safe Scintillation Chemicals for High Efficiency, High Throughput Counting

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ABSTRACT

For the last 35 years, the choice of solvent, fluor, and emulsifier for scintillation cocktails has been dictated by the need for efficient energy transfer between the beta electron and the final photon-emitting species. The modern scintillation counting laboratory has several additional requirements which make the design of a scintillation cocktail more critical than ever before: a wide variety of samples, the chemical environment of the radiolabeled sample, and the trend toward microvolume analysis. Furthermore, new environmental regulations are dramatically increasing disposal costs, making the use of high flash point, environmentally safe cocktails quite attractive. These factors combine to create the need for new types of scintillation chemicals capable of safe, high efficiency, low-volume counting. Additionally, the development of many new beta counting assays requires scintillators that are directly suitable for these applications. These requirements have lead to the development of a new generation of liquid cocktail. Data are presented indicating that this formulation provides superior counting performance, while offering a high degree of safety. Additionally, the novel characteristics of this cocktail are discussed with regard to new instrument technologies.

INTRODUCTION

The design of commercial liquid scintillation cocktails has, for many years, been based on the technical requirements of those investigators using the chemicals. These include high radionuclide counting efficiencies, large sample holding capacity, and superior resistance to quench.[1] Issues of chemical safety, storage, and disposability were assigned a relatively minor importance. The solvent used as the cocktail base plays a critical role in determining overall cocktail performance with regard to the above parameters. Acceptable results have classically been achieved with lower order benzene derivatives such as toluene, xylene, and 1,2,4-trimethylbenzene.[2]

In recent years, occupational health and safety and environmental issues have attracted much attention, both in the media and the scientific community. State and federal regulations regarding shipping, use, storage, and disposal of hazardous chemicals are increasingly stringent. Scintillation cocktails, because of the solvents cited above, are recognized as potential environmental and health hazards. As a result, considerable effort has been made to develop scintillation chemicals which offer greater safety.[3]

One of the first significant breakthroughs involved the use of a higher order benzene derivative as the solvent. Optifluor, manufactured by Packard Instrument Company, is based on a long-chain phenylalkane. The use of this solvent permitted the cocktail to be designated as nonflammable, nonhazardous, and drain disposable. However, because of the solvent low scintillation yield, counting efficiencies are less than those of conventional cocktails. The cocktail is also somewhat less quench resistant.

The most recent development is a cocktail possessing all of the characteristics necessary for superior counting performance. Ultima Gold, developed by Packard, is based on a new solvent known as diisopropylnaphthalene.[4] This solvent also has a very high flash point. As a result, Ultima Gold has been classified as nonflammable. The cocktail has been approved for drain disposal, thus reducing many of the costs associated with LS counting. Finally, Ultima Gold presents no unusual, chronic, or severe health hazards to laboratory personnel, and has no noxious or unpleasant odors associated with it.

Of greater significance is that diisopropylnaphthalene, being a derivative of naphthalene, retains the properties of a primary scintillator, while existing in a liquid form. Additional fluors and emulsifiers are readily miscible in the solvent, creating a high performance universal cocktail. The resulting formulation provides high sample capacities, with excellent quench resistance. Due to the scintillating nature of the solvent, excellent counting efficiencies are maintained even with high sample loads or the presence of tissue solubilizers.

The scintillating properties of diisopropylnaphthalene have broad implications for cocktails based on this solvent and, more importantly, liquid scintillation counting equipment. Experimental evidence suggests that the pulse shapes and fluorescent decay characteristics of cocktails based on diisopropylnaphthalene differ markedly from those of conventional cocktails and from thermal noise generated within the PMT. These differences can be used with patented time resolved pulse discrimination circuitry to provide single PMT counting systems capable of high efficiency and low background.[5] One existing application for such a combination is the use of radiochromatography systems, where a radiolabeled HPLC effluent is mixed with scintillation cocktail and presented in front of a single-PMT detector for quantitation.

This chapter summarizes accumulated data on each of the above classes of liquid scintillation cocktails. Experimental results are described which confirm the performance of these new cocktails. Furthermore, data are presented suggesting that Ultima Gold can be effectively used as a liquid cocktail in a single PMT detection system.

Table 1. General Solvent Data

Solvent	Boiling Point°C	Flash-Point°C	TLV ppm	Vapor Pressure 25°C mmHg	CLASSIFICATION International	U.S.A.	Scintillation Yield
Dioxane	101	11	50	40	Flammable liquid	Flamm. class. IB	
Toluene	110	4	100	28	Same	Same	100
Xylene	137–139	25	100	8	Same	Flamm. class. IC	110
Cumene	152	31	50	5	Same	Combustible class. II	100
Pseudo-cumene	168	50	25	2	Same	Same	112
Tri-methyl-benzenes	166–178	50	100	2	Same	Same	100
Phenyl cyclohexane	235–236	100	n.a.		Harmless chemical	Combustible class. IIIB	103
Phenyl alkane (alkylbenzene)	290–310	130–150	n.a.	0.76	Same	Same	94
Phenylxylyl ethane	302–309	150	n.a.	<1	Same	Same	110
Diisopropyl naphthalene	290–299	132–140	n.a.	1,1	Same	Same	112

EXPERIMENTAL

Physical constants, classifications, and characteristic data of solvents typically used in scintillation cocktails were compiled.[6–9] These are summarized in Table 1.

To evaluate the counting efficiency obtainable from a variety of LS cocktails, 50 μL of ^{3}H-labeled thymidine was spiked into 10 mL samples of each cocktail. Triplicate samples were made. A second set of samples was prepared without any label, to evaluate background countrates. All samples were then assayed for ^{3}H CPM in a Tri-Carb 2250C A liquid scintillation analyzer. From these count data efficiencies and figures of merit (E^2/B) were calculated for each cocktail (Table 2).

Next, to observe the effect of increasing quench on efficiency, a series of samples were prepared in each cocktail. Samples were quenched with increasing volumes of 0.01 *M* PBS, and spiked with a known and constant amount of

Table 2. LSC Efficiencies and Figures of Merit

Cocktail	Solvent	Classified as safe	Percent tritium efficiency	Bkgrd cpm	FOM E^2/B
Insta-Gel XF	Pseudocumene	No	55.3	14.4	212
Optifluor	Phenylalkane	Yes	48.4	13.4	175
Ultima gold	Diisopropyl-naphthalene	Yes	56.4	13.8	231

^{3}H-labeled water. Each was assayed for count rate in the aforementioned LSC. The results of this assay are illustrated in Figure 1.

To explain the performance of the Ultima Gold formulation, electronic signals produced at the anode of the PMT were observed and recorded on a digitizing oscilloscope. Figure 2 displays typical pulses for both Ultima Gold and PMT thermal noise.

The significant differences between these pulses suggests that time-resolved techniques can be used to discriminate against PMT noise, while retaining adequate counting efficiency. Therefore, another set of samples, similar to the ones prepared for the first set of experiments, were prepared. The assay was repeated in an experimental counting system. This system is composed of a single PMT and a pulse discrimination circuit based on time resolution. Table 3 summarizes the results of this experiment.

RESULTS AND CONCLUSIONS

While LS cocktails based on benzene derivatives offer generally excellent performance, most are characterized by some degree of environmental or safety hazard. A comparison of pertinent physical constants and data for these solvents indicates that, in some cases, these hazards and associated costs are significant. This has lead to the development of cocktails based on safe solvents. However, the data presented above suggest that the performance of these cocktails is inferior to xylene or pseudocumene based formulations. Counting efficiencies can be 10–15% lower, leading to a corresponding decrease in figure of merit. Additionally, the poor scintillation energy transfer qualities of the solvents result in cocktails which are easily and severely quenched.

The use of a new class of solvent—diisopropylnaphthalene—results in a cocktail whose counting performance meets or exceeds that of earlier safe cocktails. In fact, the results presented above suggest that this new cocktail (Ultima Gold) performs better than even cocktails based on benzene derivatives. Counting efficiencies can be somewhat higher, resulting in a 5–10% increase in figure of merit. Because diisopropylnaphthalene has scintillation properties of its own, efficient energy transfer is maintained even at extreme sample loading conditions, resulting in a cocktail with excellent quench resistance. Furthermore, this cocktail meets or exceeds all current environmental and safety requirements. Drain disposability also aids in reducing laboratory costs.

Experimental evidence gathered during these studies indicates that Ultima Gold has unique scintillation properties. The width of a typical electronic pulse produced by the interaction of a beta decay event with Ultima Gold is significantly longer than noise pulses produced in the PMT itself. We have seen differences of a factor of four. This is apparently due to the scintillating nature

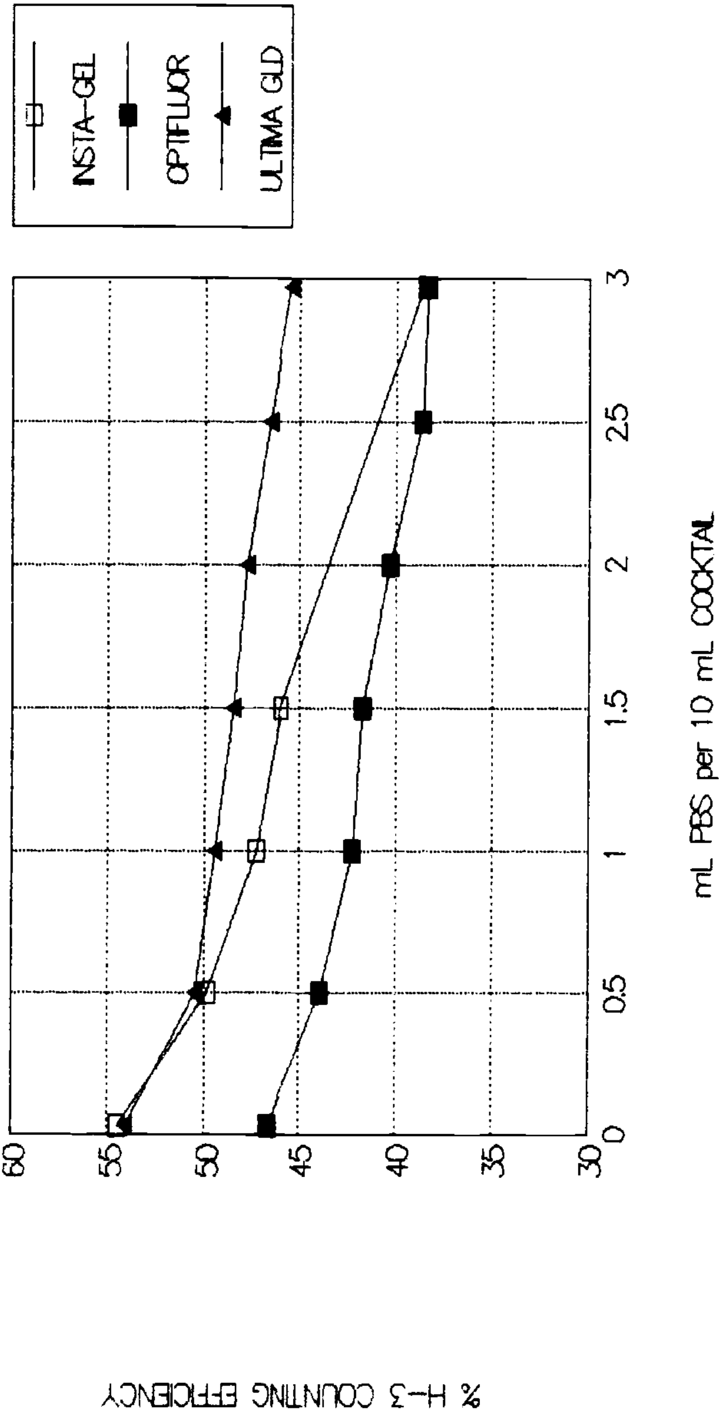

Figure 1. Cocktail quench resistance (^3H, 0.01 *M* PBS quencher).

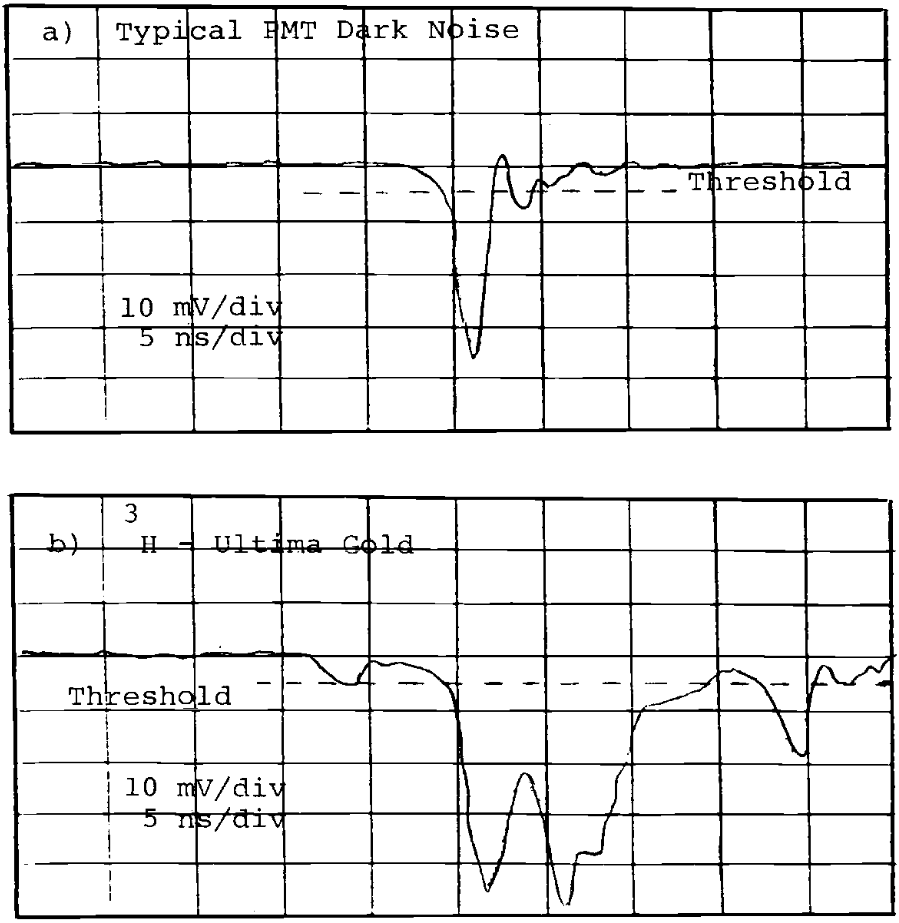

Figure 2. Electric pulses, a) PMT thermal noise, b) Ultima Gold (^3H).

of the solvent, which effectively prevents quenching of the slow component of the fluorescent decay.

As has been demonstrated, these differences in pulse width can be exploited in the use of time-resolved noise discrimination techniques. This technology

Table 3. Single PMT Counting Results

Cocktail	Solvent	Classified as safe	Percent tritium efficiency	Bkgrd cpm	FOM E^2/B
Insta-Gel XF	Pseudocumene	No	20.0	114.0	3
Optifluor	Phenylalkane	Yes	14.0	47.0	4
Ultima gold	Diisopropyl-naphthalene	Yes	32.0	54.0	19

offers the possibility of single PMT scintillation counting systems. These systems were not previously feasible with conventional liquid cocktails because of the insignificant differences between decay and noise pulses. Results in an experimental counting system based on these principles show that improvements in efficiency range from 30–60% when Ultima Gold is used. This results in a factor of five improvement in figure of merit. While efficiencies and sensitivities using this technology are somewhat less than in conventional LSC, further developments in both electronics and chemicals are expected to lead to improved performance. Furthermore, the use of time-resolved single PMT technology can lead to the development of high performance multidetector liquid scintillation counting systems.

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