International Journal of Pharmaceutical Research and Applications
Volume 8, Issue 3 May-June 2023, pp: 1858-1868www.ijprajournal.com ISSN: 2249-7781

A Reviewon Sunscreen Safety and Efficacy of skin

1.Madake Dhiraj Uddhav, 2. Swagati Moon
PratibhataiPawar college of Pharmacy, Shrirampur – 413739.

Submitted: 15-05-2023 Accepted: 30-05-2023

ABSTRACT :-
The use of sunscreen products has been advocated by many health care practitioners as a means to reduce skin damage produced by ultraviolet radiation (UVR) from sunlight. There is a need to better understand the efficacy and safety of sunscreen products given this ongoing campaign encouraging their use. The approach used to establish sunscreen efficacy, sun protection factor (SPF), is a useful assessment of primarily UVB (290-320 nm) filters. The SPF test, however, does not adequately assess the complete photoprotective profile of sunscreens specifically against long wavelength UVAI (340-400 nm). Moreover, to date, there is no singular, agreed upon method for evaluating UVA efficacy despite the immediate and seemingly urgent consumer need to develop sunscreen products that provide broad-spectrum UVB and UVA photoprotection.
With regard to the safety of UVB and UVA filters, the current list of commonly used organic and inorganic sunscreens has favorable toxicological profiles based on acute, subchronic and chronic animal or human studies. Further, in most studies, sunscreens have been shown to prevent the damaging effects of UVR exposure. Thus, based on this review of currently available data, it is concluded that sunscreen ingredients or products do not pose a human health concern. Further, the regular use of appropriate broad-spectrum sunscreen products could have a significant and favorable impact on public health as part of an overall strategy to reduce UVR exposure.

I. INTRODUCTION :-

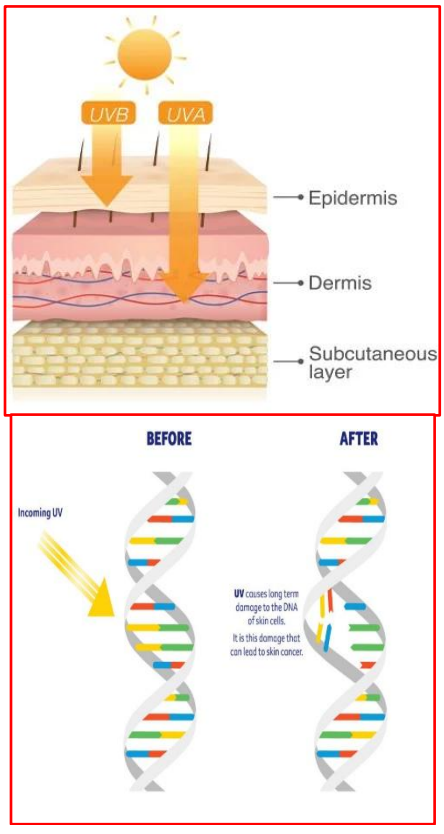
The incidence of nonmelanoma and melanoma skin cancershas been increasing in most parts of the world for severaldecades. Exposure to UV radiation (UVR)? from thesun plays a causal role in acute and chronic skin damageincluding skin cancers . As such, the medical communityand other health care providers have advocated a photoavoidancestrategy consisting of limiting sunlight exposurebetween midday hours of 1100 and 1500, wearing protectiveclothing and using sunscreens. Because sunscreens preventsunburn and their use is encouraged, it has been suggestedthat sun exposure may actually be prolonged because usersbelieve they are protected and therefore will spend moretime in the sun. This potential consequence raises severalancillary concerns. For example, because most sunscreensare primarily UVB (290-320 nm) and, in some cases, shortwavelength UVAII (320-340 nm) filters, then use of suchproducts changes the UVR spectrum to which the skin isexposed. Consequently, if behavior is modified by sunscreenuse resulting in longer periods of sun exposure, then the doseof long-wavelength **UVR,** 340 nm and above, would be increased.Further, even though sunscreens prevent sunburn,little is known regarding the threshold or dose-response forUVR-induced effects on other endpoints such as immunosuppressionor DNA damage. Finally, because sunscreensare becoming widespread and available, questions have beenraised regarding their long-term safety, particularly in thepresence of UVR. The intent of this review is to addressthese concerns, when possible, with direct evidence and discussways that sunscreen products might be improved. Tothis end, it seems necessary to examine some basic conceptsregarding the complexities of UVR and its effects on skin.After considering the effects of UVR on unprotected skin,the consequences of introducing sunscreens into this intricateinteraction will be reviewed.

EFFECTS OF SOLAR UVR ON THE SKIN :-

International Journal of Pharmaceutical Research and Applications
Volume 8, Issue 3 May-June 2023, pp: 1858-1868www.ijprajournal.com ISSN: 2249-7781

Exposure to UVR has pronounced acute, chronic or delayedeffects on the skin. The UVR-induced skin effects manifestas acute responses such as inflammation, **i.e.**sunburn**,**pigmentation (**,** hyperplasia ,immunosuppression and vitamin D synthesis), and chronic effects,primarily photocarcinogenesis and photoaging . These acute and chronic effects are dependent on thespectrum and cumulative dose of UVR; however, the completeaction spectrum for the majority of UVR-induced effectshas not been completely defined in human skin. In addition,and quite importantly, these responses have differentthresholds such that the prevention of UVR-induced changesfor one endpoint does not guarantee a similar level of protectionfor any other. Regardless, it should be kept in mindthat exposure to UVR always produces more skin damagein unprotected than in sunscreen-protected skin because theacute and chronic effects of UVR are dose, time and wavelengthdependent **(3),** and in the most empirical terms sunscreensreduce the dose of UVR.

Evidence for a role of UVR in skin cancers :-



Exposure to UVR from sunlight probably causes NMSC,based in part on the following evidence:

- People with xeroderma pigmentosum, a genetic diseasewith defective DNA repair, are exquisitely sensitive to UVRand develop NMSC at an early age predominantly on sunexposedparts of the body.
- The incidence of NMSC is inversely related to latitudein populations of mainly European origin and is greaterin outdoor compared to indoor workers.
- The NMSC is most common on the head, neck, armsand hands, areas of the body that receive the largest dose ofUVR .
- Persons that easily sunburn, **i.e.**Fitzpatrick skin typesI and 11, are more susceptible to the development of NMSC
- Mutations in the p53 tumor suppressor gene have beenfound in 90% of squamous and 50% of basal cell carcinomas,most of which are UVR signature mutations

Evidence for a role of UVR in photoaging :-

Like skin cancer, chronic exposure to solar UVR is thoughtto accelerate aging of human skin. This skin photoaging ischaracterized by dryness, roughness, irregular pigmentationsuch as freckling/lentigenes, actinic keratoses, wrinkling,elastosis, inelasticity and sebaceous hyperplasia (24). Theincidence and severity of skin photoaging are believed to bea function of cumulative UVR exposure, based on humanand animal studies. For example, Caucasian women withexcessive sun exposure have a higher incidence of photoagingthan women with a low UVR exposure history .

In addition, signs of photodamage specifically on the faceare absent in unexposed skin, **e.g.**inner portion of the arm,**of** the same individual **(38).** Importantly, photoaging differsfrom chronological or intrinsic aging of the skin and may beslowed or reversed by reduction in UVR exposure as is thecase with sunscreens or, perhaps, with other treatments suchas all-trans-retinoic acid

SUNSCREENSASPARTOFAPHOTOPROTECTION STRATEGY:-

Sunscreen-mediated photoprotection is concerned with thereduction of exposure to UVR, specifically UVB and UVA,primarily from the sun. There are two categories of sunscreenagents: organic and inorganic. The organic sunscreensare referred to as soluble or chemical sunscreens. The

International Journal of Pharmaceutical Research and Applications
Volume 8, Issue 3 May-June 2023, pp: 1858-1868www.ijprajournal.com ISSN: 2249-7781

inorganicsunscreens are commonly known as physical, mineral,insoluble, natural or nonchemical. The term nonchemicalis an obvious misnomer that has gained some consumer

Table 1. List of UVR filters used in the United States skin care market

UV filter (approximate rank order)	Comment
Octyl methoxycinnamate (OMC)	Found in over 90% of sunscreen products used in the world
Oxybenzone	Combined with OMC in many beach products
Octyl salicylate	Used in oxybenzone/OMC primarily for its solvent properties
Octocrylene	Found in many recreational sunscreen products
2-Phenyl-benzimidazole-5-sulfonic acid (PBSA)	Used in combination with OMC in daily UV protectant products
Methyl anthranilate	
Homosalate	
2-Ethylhexyl-o-dimethylamino Benzoate (Padimate O)	
Avobenzone	Currently four products
Zinc oxide	Recently approved category I sunscreen
Titanium dioxide	
p-Aminobenzoic acid (PABA)	Rarely used
Glyceryl aminobenzoate	Rarely used
Amyl *p*-dimethylamino-benzoate (Padimate A)	Rarely used
Ethyl 4 [bis(hydroxypropyl)] amino	Rarely used
Dioxybenzone	Rarely used
Sulidobenzone	Rarely used
Cinoxate	Rarely used
Diethanolamine *p*-methoxycinnamate	Rarely used
Lawsone + dihydroxyacetone (DHA)	Rarely used

Organic sunscreens:-

Organic sunscreens have been the mainstay of sunscreen formulationfor decades and, although inorganic sunscreens aregaining in popularity, organic sunscreens are still used ingreater amounts. Organic sunscreens are often classified asderivatives of (1) anthranilates, (2) benzophenones, (3) camphors,(4) cinnamates, dibenzoylmethanes, (6) p-aminobenzoatesor (7) salicylates . These aromatic compoundsabsorb a specific portion of the UVR spectrum that is generallyre-emitted at a less energetic, longer wavelength, **ie .**heat or light, or used in a photochemical reaction, such as**cis-trans** or keto-enol photochemical isomerization .

Inorganic sunscreens:-

During this decade, the inorganic sunscreens have been usedwith increasing frequency in beach and daily use photoprotectionproducts. This has been driven, in part, by their safetyand effectiveness, particularly in blocking **UVA,** and theconcern regarding potential adverse effects of organic sunscreens.The inorganic sunscreens are generally viewed asharmless pigments that cannot enter the skin and are largelyunaffected by light energy like organic sunscreens may be.

The two most commonly used inorganic sunscreens are titaniumdioxide (Ti02) and zinc oxide (ZnO). Although thesetwo metal oxides differ substantially in their appearance andattenuation spectra (42), they share some general propertiesthat are discussed briefly.

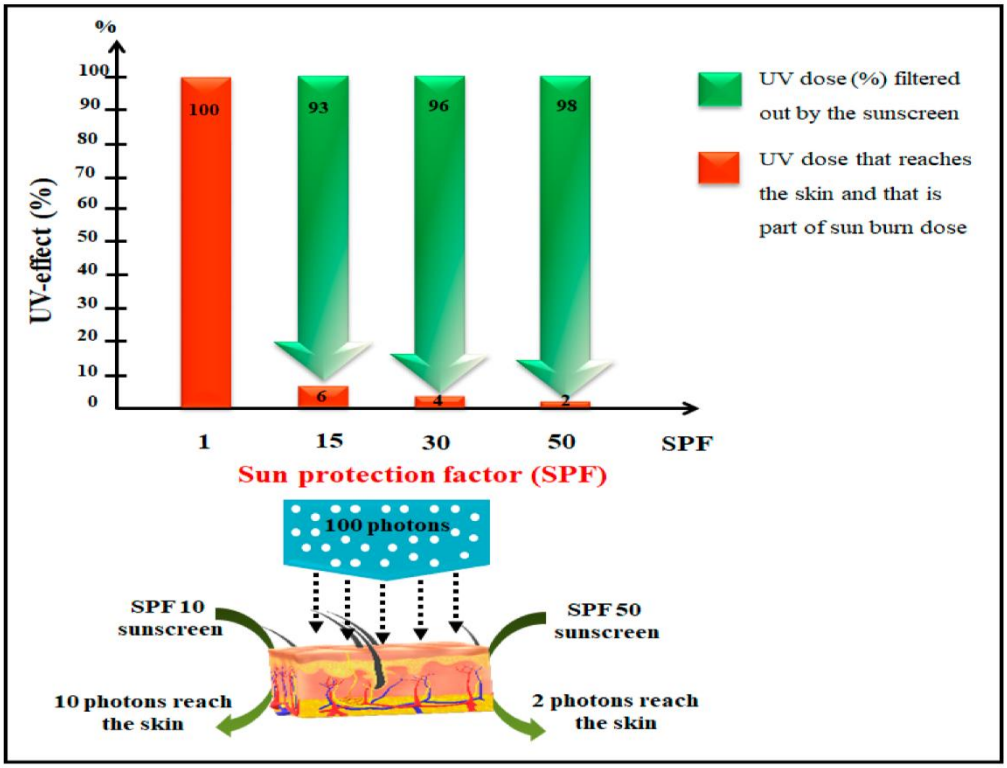
Zinc oxide and TiO, exist as odorless white powders comprisedof a Gausian or normal distribution of particle sizes.Microfine powders, used in sunscreen products, have an averageparticle size of approximately 0.20 pm (micron) orless with a distribution that **is** narrow and well controlled.Importantly, compared to the traditional pigment grades ofthese metal oxides that have been used for years in cosmeticproducts, microfine powders do not contain smaller particles,rather the lower end of the normal particle size distributionis augmented through specialized manufacturing procedures.In other words, microfine powders have always been presentin ZnO- or Ti0,-containing products but were optically overwhelmedby the larger particles. Thus, microfine particles donot

International Journal of Pharmaceutical Research and Applications
Volume 8, Issue 3 May-June 2023, pp: 1858-1868www.ijprajournal.com ISSN: 2249-7781

represent an entirely new particle size, just a refinementof the existing particle size distribution (43).

Each particulate has a size at which it maximally scattersvisible light (43). This is the ideal size for use as a white orcolored pigment. **As** a sunscreen, however, any color renderedto the product by an ingredient is undesirable. Thus,the average particle size of a metal oxide is reduced belowthe optimal light scattering size, allowing visible light to betransmitted and therefore, appearing virtually invisible onthe skin. This property has been employed to yield the microfinegrades of metal oxides that are now being widelyused in sunscreen and daily skin care formulations.

SUNSCREEN EFFICACY:-



Sunscreens represent unique products because, if appliedproperly, their efficacy is guaranteed. This guarantee isbased on their ability to prevent sunburn, which has beenthe criterion used to evaluate these products to date. As presentedin this paper, however, this singular criterion does notappear to be sufficient for evaluation of sunscreen productsin the future. This view is based on the need for broadspectrumUVB and UVA photoprotection products. Nonetheless,unlike any other OTC drug, the final sunscreen productis tested for efficacy before consumer distribution. Themethods used to evaluate the efficacy of sunscreens will bebriefly conside

SPF: A measure of protection against UVB

There is no question regarding product efficacy-sunscreensprevent sunburn. The selection of a sunscreen or combinationof sunscreens and the resultant formulation is designedand evaluated for this purpose. The SPF for a sunscreen isdefined as the ratio of sun exposure that skin can tolerateb**e**fore burning or minimal erythema **i s** apparent with andwithout sunscreen protection. Thus, SPF is really the protectionfactor for sunburn.

Because the action spectrum for UVR-induced sunburn issimilar to that for a specific measure of DNA damage, itoften has been inferred that protection against sunburn is thesame as protection against DNA damage and a host of otherendpoints as well. However, as mentioned previously, it isnow clear that each biological response has a unique actionspectrum and even

International Journal of Pharmaceutical Research and Applications
Volume 8, Issue 3 May-June 2023, pp: 1858-1868www.ijprajournal.com ISSN: 2249-7781

when different responses have similaraction spectra the threshold or dose-response or both toUVR may differ dramatically (3,14,17,19-23,39). Thus, althoughSPF provides a measure of sunburn protection, itsvalue for other endpoints is limited and could be viewed asmisleading

SUNSCREEN SAFETY

Besides traditional recreational and daily photoprotectionproducts, sunscreens are increasingly included in diverseconsumer products. Given this, questions regarding theirlong-term safety, particularly in the presence of UVR exposure,have been raised. The intent of this section, therefore,is to address some current concerns regarding sunscreensafety. This is not a comprehensive review of thepublished studies on sunscreen safety, rather an attempt tocompare and contrast results of in **vitro** studies with thoseobtained in vivo.

It is important to distinguish between long-term safetyconcerns and short-term adverse reactions. Sensitivities, bothphoto- and nonphotoinduced, to organic sunscreens are welldocumented and seemingly rare events, although there arefew published studies making it difficult to know the actualprevalence (49-5 1). These important and meaningful eventslikely impact compliance but do not represent the sort oflong-term toxicity issues we discuss in this paper.

In general terms, the toxicological evaluation of any

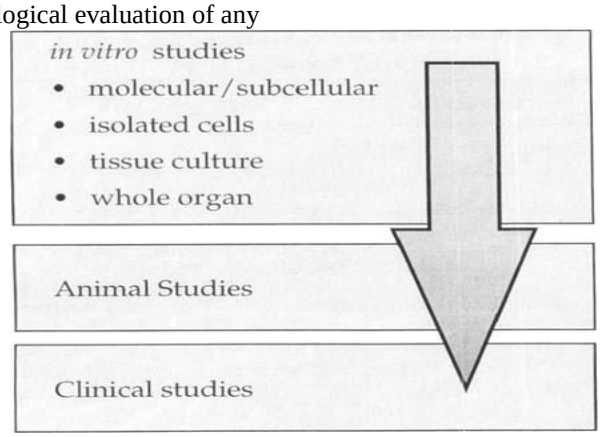


Figure 1. Toxicological hierarchy in assessment of human **risk.**

Thiscartoon represents different levels of human relevance from a toxicologicalviewpoint. Results from **in vitro** studies need to be balancedagainst animal and clinical studies when considering risk tohuman health.

chemical where human exposure is likely often includesshort-term **in vitro** studies that are believed to be predictiveof long-term or delayed toxicity. This is quite evident in thecarcinogenic risk assessment of chemicals where bacteriamutation assays have become a mainstay in this process.With regard to sunscreens, assessment of the mutagenic potentialrepresents a unique challenge considering their specificfunction, namely absorption of UVR. As such, shortterm**in vitro** approaches measuring various endpoints havebeen conducted with sunscreens, many of which includeUVR exposure. In general, these are cytotoxicity or genotoxicity,**i.e.**bacteria mutagenicity and mammalian cell clastogenicitystudies that include concurrent UVR exposure.

The photogenotoxicity testing of a chemical is judgedagainst results obtained with a positive control, 8-MOP. Because8-MOP is the only demonstrated human photocarcinogenknown, the assessment of any compound using these**in vitro** tests is tenuous at best. Nonetheless, there are anumber of studies examining the acute interaction betweenUVR and chemicals for both organic and physical sunscreens.In general, these studies have been conducted toidentify what effects sunscreens have on UVR-induced damage,either genetic or cytotoxic, and, by inference, UVRinducedskin carcinogenesis. This strategy remains in theinfant stages of development, although to date, this approachappears to have little bearing on human safety assessment.Finally, when evaluating the human safety of sunscreensand other xenobiotics, it is important to understand the hierarchical

value of the experimental results. For example,studies conducted in humans provide direct evidence in thespecies of interest thereby eliminating issues regarding extrapolationand

International Journal of Pharmaceutical Research and Applications
Volume 8, Issue 3 May-June 2023, pp: 1858-1868www.ijprajournal.com ISSN: 2249-7781

relevance inherent in animal and **in vitro** investigations.

Similarly, studies conducted in animals providean integrated response resembling the human circumstancemore closely than **in vitro** single cell studies. This hierarchicalprioritization, crudely illustrated in Fig 1

Studies with organic sunscreeens

p-Aminobenzoic acid (PABA) was patented in 1943 and formany years was the primary organic sunscreen active used.

Derivatives of PABA including **2-ethylhexyl-o-dimethylam**inobenzoate(Padimate 0) and amyl p-dimethylaminobenzoate(Padimate A) were developed and utilized during the1960s and 1970s. Since then a number of other sunscreenagents have become available, several with reduced probabilityof photorelated toxicity making PABA and its derivativesrarely used sunscreens. Despite its infrequent use,PABA has been the subject of much research**Acute** in vivo **studies.** From the **in vitro** study resultabove, it is apparent that under specific artificial conditions,organic sunscreens, predominantly PABA and its derivatives,can interact with DNA following UVR either directlyor indirectly. The effect of PABA and other organic sunscreenson measures of DNA damage produced by acuteexposure to UVR has been evaluated **in vivo** using primarilyhairless mice. Walter (67) and Walter and DeQuoy (68)found that several organic sunscreens including PABA andits derivatives reduced UV-induced DNA damage in the skinof hairless mice. More recently, Ley and Fourtanier (69)reported that octyl methoxycinnamate (OMC), the mostcommon UVB sunscreen used in the world, and terephthalylidenedicamphor sulfonic acid, a UVBAJVA filter, reducedthe number of UV-induced pyrimidine dimers in epidermalDNA of hairless mice exposed to SSR.

Most recently, studies investigating UVR-induced mutationsin the p53 tumor suppressor gene have been conducted.As stated earlier, it has been reported that the p53 tumorsuppressor gene is mutated in 90% of squamous cell carcinomasand 50% of basal cell carcinomas from human subjects(31). Ananthaswamy**et** al. (70) described the ability ofsunscreens, one containing the UVB filters octocrylene and**2-phenylbenzimidazole-5-sulfonic** acid and the other containingthe same UVB filters plus UVA filters avobenzoneand terephthalylidenedicamphor sulfonic acid, to inhibit theinduction of p53 mutations in UVR-irradiated C3H mouseskin. In order to avoid the tedious task of examining all 11exons of p53, these authors selected a site that is mutated in27% of UV-induced skin tumors in mice for sequence analysis.

They showed that the application of sunscreens beforeeach irradiation nearly abolished the occurrence of p53 mutationsat the selected site. In these studies artificial lightemitting only a portion of the solar spectrum was employed,which means that these mice were not exposed to the highdoses of longer wavelength UVA and shorter wavelengthvisible light that is contained in the solar spectrum. Nonetheless,this is an important study because it examined theeffects of sunscreens on a molecule that influences the fateof a cell

International Journal of Pharmaceutical Research and Applications
Volume 8, Issue 3 May-June 2023, pp: 1858-1868www.ijprajournal.com ISSN: 2249-7781

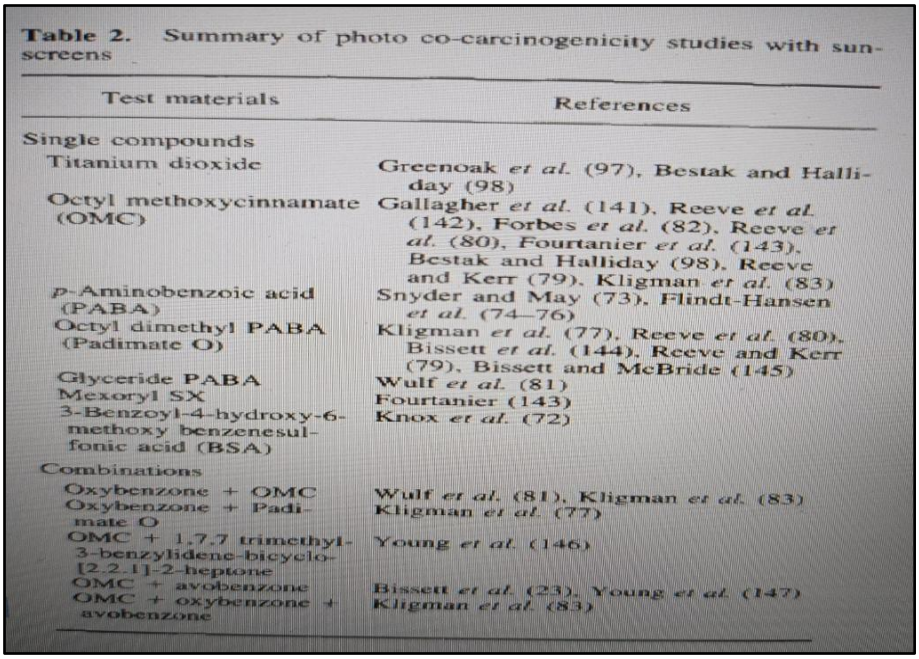


Table 2. Summary of photo co-carcinogenicity studies with sunscreens

Test materials	References
Single compounds	
Titanium dioxide	Greenoak *et al.* (97), Bestak and Halliday (98)
Octyl methoxycinnamate (OMC)	Gallagher *et al.* (141), Reeve *et al.* (142), Forbes *et al.* (82), Reeve *et al.* (80), Fourtanier *et al.* (143), Bestak and Halliday (98), Reeve and Kerr (79), Kligman *et al.* (83)
p-Aminobenzoic acid (PABA)	Snyder and May (73), Flindt-Hansen *et al.* (74–76)
Octyl dimethyl PABA (Padimate O)	Kligman *et al.* (77), Reeve *et al.* (80), Bissett *et al.* (144), Reeve and Kerr (79), Bissett and McBride (145)
Glyceride PABA	Wulf *et al.* (81)
Mexoryl SX	Fourtanier (143)
3-Benzoyl-4-hydroxy-6-methoxy benzenesulfonic acid (BSA)	Knox *et al.* (72)
Combinations	
Oxybenzone + OMC	Wulf *et al.* (81), Kligman *et al.* (83)
Oxybenzone + Padimate O	Kligman *et al.* (77)
OMC + 1,7,7 trimethyl-3-benzylidene-bicyclo-[2.2.1]-2-heptone	Young *et al.* (146)
OMC + avobenzone	Bissett *et al.* (23), Young *et al.* (147)
OMC + oxybenzone + avobenzone	Kligman *et al.* (83)

One of the first published studies examining the ability ofsunscreens to inhibit UVR-induced skin cancer in rodentswas the work of Knox **et** al. (72). They conducted a seriesof experiments with mice to determine the effect of a benzophenonederivative, **3-benzoyl-4-hydroxy-6-methoxyben**zenesulfonicacid (BAS), or PABA on the development ofskin cancer produced by artificial UVR. Both BAS andPABA were found to decrease UVR-induced tumor formation.

Consistent with these results are the studies by Snyderand May (73) and Flindt-Hansen **et** al. (74,75) that foundtopical treatment with PABA significantly reduced the tumorigeniceffects of UVR in mice. Furthermore, Flindt-Hansen**et** al. (76) demonstrated that preirradiated, photodegradedsolutions of PABA still protected mice against UVR-inducedtumor formation. Thus, in contrast to **in vitro** resultsdemonstrating enhancement of UVR dimer formation orphotomutations that lead to the logical hypothesis thatPABA would enhance UV-induced tumorigenesis, these **invivo** data convincingly demonstrate that this sunscreen protectsagainst UVR-induced tumor formation in mice

Studies with inorganic sunscreens:-

Although metal oxides, TiO, and ZnO, have been used foryears in consumer products and are generally considered tobe inert, recent photocatalytic applications of TiO, (84,85)have led some to a reconsideration of their effect in sunscreens.

TiOz is a semiconductor that can absorb light andunder certain conditions generate free radicals (43,44,78).The band gap (3 eV for Ti02) is a measure of the minimumenergy in electron volts required to promote an electron fromthe valence band to the conduction band. A compound witha band gap in the region of 3 eV can be excited by radiationat wavelengths below -380 nm. Thus, TiO, may be susceptibleto excitation by UVB and UVA in sunlight. Photoexcitationof TiO, could promote a single electron from thevalence band to the conduction band, leaving a positivelybineswith the hole, but sometimes the hole migrates to thesurface of the particle, where it can react with absorbed species.

In an aqueous environment it can react with water orhydroxyl ions, forming hydroxyl radicals (86). Such processesare well known for aqueous preparations of TiO, exposedto either artificial UV light or natural sunlight. In thiscapacity, the photocatalytic potential of TiOz has been usedexperimentally to degrade suspensions of organic materialsand purify drinking water (87).

Considering the photocatalytic potential of metal oxides,it has been proposed as well that a photoreactive pigment ina sunscreen product may degrade organic UVR filters alsopresent in the formula. This has been studied using commerciallyrepresentative sunscreens that contained both organicand inorganic sunscreens (88). Thin films of the sunscreenswere applied to a synthetic substrate and irradiatedwith increasing

International Journal of Pharmaceutical Research and Applications
Volume 8, Issue 3 May-June 2023, pp: 1858-1868www.ijprajournal.com ISSN: 2249-7781

doses of solar-simulated UVR, the highestdose being 30 J/cm2. The sunscreen and substrate were digestedand the percent organic sunscreen remaining was determined.

Both coated, microfine ZnO and TiO, were shownto be photoprotective with respect to the organic sunscreensoctyl methoxycinnamate and avobenzone. Similar resultswere obtained with uncoated microfine ZnO as well. Thesedata show that, in finished formulation, these metal oxidesnot only caused no detectable break down of adjacent organicmolecules but actually improved their survival.Chronic in vivo studies. The hypothesis that Ti02 mayenhance UVR-induced damage has been investigated inchronic photocarcinogenicity studies in mice. In two separatestudies, it was found that micronized TiO, substantiallyreduced UVR-induced tumor formation in mice (97,98).These data are consistent with the acute in vivo results anddiametrically opposed to the seemingly logical extension ofthe in vitro studies. Simply stated, the in vitro studies do notpredict chronic in vivo findings. Thus, considering the worstcase using the most photocatalytically active metal oxide,TiO,, there is no evidence that repeated application in thepresence of UVR represents a potential human hazard underthe conditions of these studies. To the contrary, in vivo experimentshave shown the topical application of metal oxidesas sunscreens to be beneficial.

Sunscreen studies in humans:-

Acute studies. The effect of sunscreens on the acute effectsof UVR has been assessed in human skin. For example,Freeman **et** al. (99) found that a sunscreen containing OMCand benzophenone-3 protected human skin from UVR-inducedDNA damage as evaluated by formation of pyrimidinedimers. The study by van Praag**et at.** (100) found a sunscreencontaining the UVA filter, avobenzone, and the UVBfilters, **3-(4'-methylbenzy1idene)-camphor** and 2-phenyl-benzimidazole-5-sulfonic acid, prevented UVB-induced cyclobutanedimer formation in human skin. Finally, PABA significantlyreduced unscheduled DNA synthesis produced byhigh dose, 2 minimal erythema dose (MED), UVR exposurein human skin (101). Collectively, these data showing preventionby sunscreens of acute UVR-induced DNA damagein vivo support their protective benefit in humans. Moreover,despite the diverse methods and different endpoints, a singularfavorable outcome was obtained.

Chronic studies. There is no direct evidence in humansthat sunscreen use prevents nonmelanoma or melanoma skincancers primarily due to the inability to conduct such a protractedstudy. However, in two prospective clinical studiesit was found that repeated use of sunscreens suppresses thedevelopment of precancerous lesions **(ie.** actinic or solarkeratosis). Thompson et al. (104) found that regular use ofa sunscreen containing OMC and avobenzone (tert-butyldibenzoylmethane)for 7 months prevented the developmentof solar keratoses in a dose-dependent manner. Because solar(actinic) keratoses are precursors of squamous cell carcinomaand a risk factor for basal cell carcinomas and melanoma(103, these data are suggestive that sunscreen use reducesthe risk of skin cancers in the long term. Similarly, Nayloret **al.** (106) found that regular use of an **SPF** 29 sunscreencontaining OMC, benzophenone-3 and octyl salicylate over2 years significantly reduced cutaneous neoplasia, as indicatedby its suppression **of** precancerous lesions. These dataare the most direct evidence that use of sunscreen reducesthe **risk** of NMSC in humans. Finally, the use of sunscreenshas been reported to diminish some aspects **of** photoagingin humans (107). These data are supported by animal studiesthat have clearly established that sunscreens diminish photodamage(108-1 10). Thus, prospective clinical studies ofsunscreen use by humans have found that regular, daily usereduces measures of chronic UVR-induced skin damage.

II. DISCUSSION:-

The most apparent acute benefit of currently available sunscreensis the prevention of sunburn from UVR exposure.This effect has been suggested to be both a benefit and apotential concern. The obvious benefit is the prevention ofsunburn that may reduce the risk of nonmelanoma and perhapsmelanoma skin cancers because severity and frequencyof sunburns has been associated with NMSC formation(2,29,30). The concern has been inadequate protection ofexisting sunscreens and, more important, the potential forprolonged UVR exposure without acute signals (i.e.sunbum)ultimately leading to greater doses of UVA (1 11). Althoughthe assumption that sunscreen use promotes or encouragesprolonged sun exposure has not been substantiatedwith any data (112), it remains a popular view that is, inpart, logical and appealing. Regardless, it should be notedthat for a given acute UVR exposure, the skin damage producedin the

International Journal of Pharmaceutical Research and Applications
Volume 8, Issue 3 May-June 2023, pp: 1858-1868www.ijprajournal.com ISSN: 2249-7781

absence of sunscreen photoprotection exceedsthat obtained in their presence.

The human safety of current sunscreens:-

The most contentious views related to the safety of sunscreenshave been built on in vitro findings using preparationsof naked DNA or cultured cells. These studies havefound that following irradiation, sunscreens may attack DNAeither directly or indirectly viz u viz free radicals to producedamage in the form of adducts or cell death (56,58). Fromthese results, it has been suggested that sunscreens may contributeto long-term skin damage. Specifically, it has beensuggested that the DNA damage observed in these in vitro studies may be carcinogenic and may result when sunscreensare used as directed. If the **in vitro** mechanisms have anybasis for concern, then acute and, most important, chronicapplication should reflect these events and sunscreens should

accelerate the appearance of UVR-induced DNA damage ortumor formation **in vivo.** As demonstrated, however, the **in**vivo results provide a singular answer that sunscreens protectagainst acute and chronic or delayed UVR-induced skindamage. For example, there was a trend toward delayingUV-induced tumor formation and decreasing the number oftumors per mouse in all photo-cocarcinogenicity studies conductedwith sunscreens alone or in combination (Table 2).

The singular outcome of these studies occurred despitemethodological differences in all studies. The extent of protectionby the sunscreens ranged from complete inhibitionof UV-induced tumor formation to a delay in the appearanceof tumors by 2-3 weeks. Thus, safety concerns based oncurrent **in vitro** results with sunscreens have no bearing onthe human use of sunscreens and may, in fact, be harmfulto the extent that they discourage sunscreen use.

Protected versus unprotected skin

When one applies a sunscreen, the attenuation spectrum ofthat sunscreen defines the spectrum of UVR to which underlyingcells in the skin are subjected. In this way, sunscreensalter the light spectrum to which the skin is exposed.This sunscreen-protected spectrum **(SPS)** will depend on thekind of sunscreen used and, with the majority of sunscreenproducts currently available, it is certain that longer UVAwavelengths will comprise this SPS. It is for this reason thatideally we should know the complete action spectra, thresholdand dose-response for any physiological, biological andmolecular phenomena that occur in the skin. For example,the elucidation of skin immunology two decades ago led toa concern that even though sunscreens block the acute inflammationproduced by UVR they might not prevent theimmune-suppressive effects. Numerous studies have comedown on different sides of this question (123,124). Differentexperimental conditions, including light sources and the lackof UVC filters, can account for many of the disagreementsand the full story remains to be told because a completeaction spectrum for immune suppression has not been described.Thus, it seems critical that UVR-mediated biologicalevents be carefully characterized before the significance ofUVR-sunscreen interactions can be fully understood.

Sunscreen use and melanoma:-

It is well beyond the scope of this review to consider therole of sunscreen use and the preventiodcausation of melanoma.However, it is necessary to mention considering thecontroversies surrounding this subject. In the most simpleterms, if UVR exposure plays a role in the etiology of melanomaas suggested (2,33-35), then reducing sun exposureshould diminish the risk of developing

International Journal of Pharmaceutical Research and Applications
Volume 8, Issue 3 May-June 2023, pp: 1858-1868www.ijprajournal.com ISSN: 2249-7781

this skin cancer.Thus, sunscreens would by this definition be beneficial inreducing the risk of melanoma provided they are appliedproperly, on a regular basis and do not modify behaviorleading to prolonged periods of sun exposure. Clearly, thelack of an animal model of melanoma has slowed our abilityto understand the pathogenesis of this disease. There is anurgent need for more research in the causation of melanomaand prospective clinical studies of preventive approaches including the use of sunscreens.

The need for broad-spectrum UVBRJVA sunscreenProducts

There is growing evidence that although UVB is the mostdamaging component of sunlight, UVA is responsible fornumerous morphological, molecular and biochemical eventsthat may contribute to photodamage of skin (125-128). Theeffects of long-term UVA radiation have been reported to bedifferent qualitatively and quantitatively from those of UVB(1 29-1 3 1). Finally, the mechanism(s)/chromophores bywhich these wavelengths affect biological processes are different.For example, UVB is believed to be absorbed primarilyby DNA, RNA and proteins that may be the directchromophores mediating the damaging effects of thesewavelengths. In contrast, the effects of UVA are secondaryto the formation of free radicals, and the chromophore(s)leading to the generation of these reactive oxygen species isunknown.

REFERENCES

[1]. Bissett, D. L., J. F. McBride, D. P. Hannon and L. F. Patrick(1 99 1) Time-dependent decrease in sunscreen protectionagainst chronic photodamage in UVB-irradiated hairless mouseskin. **J.** Photochem. Photobiol. B Biol. **9,** 323-334.

[2]. Garland, C. F., F. **C.** Garland and E. D. Gorham (1993) Risingtrends in melanoma: an hypothesis concerning sunscreen effectiveness.**Ann.** Epidemiol. **3,** 103-1 10.

[3]. Stender, I.-M., J. L. Andersen and H. **C.** Wulf (1996) Sunexposure and sunscreen use among sunbathers in Denmark.**Acta** Dermato-Venereol. **76,** 31-33.

[4]. 4. Moran, C. A,, F. **G.** Mullick, K. G. Ishak, F. B. Johnson and W. B. Hummer (1991) Identification of titanium in human tissues:probable role in pathologic processes. Hum. Pathol. **22,**450454.

[5]. Dupre, A., P. Touron, J. Daste, J. Lassere, J. L. Bonafe and R.Viraben (1985) Titanium pigmentation. An electron probe microanalysisstudy. Arch. Dermatol. **121,** 656-658.

[6]. Tan, M.-H., C. A. Commens, L. Burnett and P. J. Snitch (1996)A pilot study on the percutaneous absorption of microfine titaniumdioxide from sunscreens. Australas. **J.** Dermatol. **37,**185-187.

[7]. Hallmans, G. and **S .**Liden (1979) Penetration of 6sZn throughthe skin of rats. Acta Demato-Venereol. **59,** 105-1 12.Agren, M. **S.** (1991) Influence of two vehicles for zinc oxideon zinc absorption through intact skin and wounds. **Acra**Dermato-Venereal. **71,** 153- 165

[8]. Agren, M. **S.,** M. Krusell and L. Franzen (1991) Release andabsorption of zinc from zinc oxide and zinc sulfate in openwounds. Acta Dermuto-Venereol. **71,** 330-333.

[9]. Agren, M. **S.** (1990) Percutaneous absorption of zinc from zincoxide applied topically to intact skin in man. Dermatologica**180,** 36-39.

[10]. Derry, **J.** E., W. M. McLean and J. B. Freeman (1983) A studyof the percutaneous absorption from topically applied zinc oxideointment. **J.** Parenter. **Enferal**Nutr. **7,** 131-135.

[11]. Dussert, A.-S., E. Gooris and J. Hemmerle (1997) Characterizationof the mineral content of a physical sunscreen emulsionand its distribution onto human stratum corneum. Int. **J.** Cosmet.Sci. **19,** 119-129.

[12]. Vinson, J. A. and J. Proch (1997) Age-related differences intopical zinc absorption from different formulations: implicationsfor health and disease. **J.** Geriatr. Dermatol. **5,** 276-280.

[13]. Wolf, P. and M. L. Kripke (1997) Immune aspects of sunscreens.Chapter 7. In Sunscreen Photobiology (Edited by F.P. Gasparro). Landes Press, Georgetown, TX.

[14]. Roberts, L. K. and D. B. Learn (1997) Sunscreen SPF valuesand immune protection levels are equivalent when tests areconducted by appropriate methods and procedures, Chapter 8.In Sunscreen Photobiology (Edited by F. P. Gasparro). LandesPress, Georgetown, TX.

[15]. Kligman, L. H. and M. Gebre (1991) Biochemical changes inhairless mouse skin collagen after chronic exposure to UVAradiation. Photochem. Photohiol. **54,** 233-237.

[16]. Scharffetter, K., M. Wlaschek, A. Hogg, K. Bolsen, A. Schothorst,G. Goerz, T. Krieg and G. Plewig (1991) UVA irradiationinduces collagenase in human dermal fibroblasts **in** vitro andin vivo. Arch. Dematol. Res. **283,** 506-5 1 1.

[17]. Wlaschek, M., K. Bolsen, G. Henmann, **A.** Schwarz, F. Wilmroth,P. C. Heinrich, G. Goerz and K. Scharffetter-Kochanek(1993) UVA-induced autocrine stimulation of fibroblast-derived-collagenase by IL-6: a possible mechanism in dermalphotodamage? **J.** Invest. Dermatol. **101,** 164-168.

[18]. Lavker, R. and K. Kaidbey (1997) The spectral dependencefor UVA-induced cumulative damage in human skin. **J.** Invest.Dermatol. **108,** 17-21.

[19]. Kligman, L. H., F. J. Akin and A. M. Kligman (1985) Thecontributions of UVA and UVB to connective tissue damagein hairless mice. **J.** Invest. Dermatol. **84,** 272-276.

[20]. Zheng, P. and L. H. Kligman (1993) UVA-induced ultrastructuralchanges in hairless mouse skin: a comparison to UVBinducedchanges. **J.** Invest. Dermarol. **100,** 194-199.

[21]. Kligman, L. H. (1992) UVA-induced biochemical changes inhairless mouse skin collagen: a contrast to UVB effects. InBiological Responses to Ultraviolet A Radiation (Edited by F.Urbach), pp. 209-21 5. Valdenmar Publishing, Overland Park,**KS.**