tion of the zones was made by placing the developed plates in a jar containing iodine crystals. Within 5 min. brown spots appeared. Costunolide and tulipinolide showed R_f values of 0.53 and 0.37, respectively.

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Thin-Layer and Gas-Liquid Chromatography of Some Indanol Derivatives of Pharmaceutical Interest

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Abstract □ Various solvent systems and adsorbents used in the separation and identification of indanol derivatives in TLC have been reported. Quantitative estimation of the active principle in some pharmaceutical preparations by means of GLC are also included in this work.

Keyphrases □ Indanol derivatives—separation, identification □ TLC—separation, identification □ UV light—chromatographic spot visualization □ GLC—separation, identification

Some of the indanol derivatives especially 7-chlor-4-hydroxyl indan and 4-hydroxy-1,5,7-trimethyl indan have distinguished themselves because of showing excellent bactericidal, fungicidal, and amebicidal properties *in vitro* as well as *in vivo* (1–4). These compounds can be prepared by a ring cyclization (5) reaction or by substituting the corresponding indan (6). For a qualitative as well as a quantitative control of the purity of the starting materials and end products in the pharmaceutical specialties it was necessary to conduct some TLC and GLC experiments. Not much work (7, 8) has been done on indanols in comparison to the number of publications on the chromatography of phenols. It was found worthwhile to include some of the related indan derivatives in the present investigations.

EXPERIMENTAL

Thin-layer Chromatography

Adsorbents—Silica Gel G (Woelm TLC) and polyamide (Woelm TLC) were used. In either case the adsorbent was mixed with approximately 2% fluorescent indicator green before preparing the slurry. The plates can be used after drying them overnight at room temperature.

Solvent Systems—(I) Water-saturated chloroform; (II) benzene–chloroform–absolute alcohol, 4:1:1; (III) chloroform–absolute alcohol, 97:3; (IV) benzene; (V) and carbon tetrachloride.

Detection—Thin-layer plates should be dried after development and then viewed under UV light of 254 mμ. The substances show up as dark spots against a greenish fluorescent background. In case the fluorescent indicator or a UV lamp is not available, the plates should be sprayed with an aqueous potassium permanganate (1%) solution. Yellow spots against a violet-brown background indicate the position of various compounds.

Table I—Chromatographic Data for the Indanol Derivatives

Substances	R_f Values with Silica Gel G in Solvent Systems I	II	III	IV	V	R_f Values with Polyamide in Solvent System I
4-Hydroxy indan	0.31	0.84	0.78	0.25	Start	0.74
5-Hydroxy indan	0.22	0.82	0.72	0.18	Start	0.63
7-Chlor-4-hydroxy indan	0.28	0.78	0.72	0.23	Start	0.52
5,7-Dichlor-4-hydroxy indan	0.69	0.89	0.91	0.63	0.31	0.84
7-Chlor-4-hydroxy-indan-on(1)	0.60	0.91	0.94	0.44	0.08	0.90
5-Acetyl indan	0.60	0.92	0.94	0.34	0.05	Front
5-Amino indan	0.79	Front	0.94	0.83	0.38	Front
4-Hydroxy-1,5,7-trimethyl indan	0.59	0.89	0.85	0.44	0.07	0.87

Table II—GLC Data for the Indanol Derivatives (System 1)

Substances	Retention Time, min.
4- Hydroxy indan	10.0
5- Hydroxy indan	12.8
5,7-Dichlor-4-hydroxy indan	16.0
7-Chlor-4-hydroxy indan	32.5

Results and Discussion—Table I shows R_f values on TLC plates prepared with an applicator. Separations of equally good and reproducible quality could be obtained on manually (9) prepared plates. In these experiments while benzene proved to be the most suitable solvent system with pptd. silicic acid,[1] water-saturated chloroform was the best for polyamide. The two isomers 4- and 5-hydroxy indans could be separated without difficulty. The presence of 7-chlor-4-hydroxy indan in dragees and suppositories could easily be proved.

Gas-Liquid Chromatography

During the preparation of 7-chlor-4-hydroxy indan by chlorinating 4-hydroxy indan with sulfonyl chloride two side products namely 7-chlor-4-hydroxy- and 5-chlor-4-hydroxy indans (6) have been reported. The TLC investigations of this fraction, however, showed that there were two spots, having R_f values which correspond with those of 7-chlor-4-hydroxy- and 5,7-dichloro-4-hydroxy indans. The TLC findings were confirmed by GLC results. The suspected 5,7-dichloro-derivative was isolated from the reaction mixture. A mixed melting point with an authentic sample showed no depression.

Apparatus used was: a gas chromatograph (Perkin Elmer F 6 model) with a 160-ma. thermal conductivity detector; a 1-m. steel, column, 0.636 cm. (0.25 in.) o.d. The packing was 2% ×E60 + 2% polyethylene glycol[2] (20 *M*) on Fluoropak 80. The carrier gas was helium at 60 ml./min. Temperatures were: injection port, 220°; column, 200°; and detector, 230°. Table II shows the retention times of various substances.

In a second experiment the column and the packing were changed as follows: column, steel, 2 m., 0.636 cm. o.d.; packing, 5% S.E. 30 on 80–100 mesh diatomite;[3] carrier gas, helium 80 ml./min. Temperatures were: injection port, 170°; column, 150°; and detector, 180°. Table III shows the retention times of different substances with this system.

A good separation of 4- and 5-hydroxy indans could also be achieved on a column with a packing of 15% celanese ester 9 on 60–100-mesh diatomaceous earth.[4]

[1] Silica Gel G.
[2] Carbowax.
[3] Chromosorb W.
[4] Celite.

Table III—GLC Data for Indanol Derivatives (System 2)

Substances	Retention Time, min.
4-Hydroxy indan	9.0
5-Hydroxy indan	10.4
7-Chlor-4-hydroxy-indan-on(1)	22.5
7-Chlor-4-hydroxy indan	25.5
5,7-Dichlor-4-hydroxy indan	29.5
4-Hydroxy-1,5,7-trimethyl indan	35.5

Method—For the quantitative estimation of 7-chlor-4-hydroxy indan in dragees it was necessary to powder and extract them with chloroform. This after drying and concentrating *in vacuo* was subjected to GLC. The vaginal suppositories were dissolved in ether and shaken with a 10% NaOH solution. The aqueous phase was acidified with HCl and extracted with chloroform and analyzed as in case of dragees.

DISCUSSION

For the quantitative estimation of 7-chlor-4-hydroxy indan in dragees and suppositories with GLC an accuracy of ±4% is possible. The method is simple and gives reproducible results.

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